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EVALUATION OF THE EFFECTIVENESS OF ANTI-INFLUENZA VACCINATION*

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EVER SINCE the first influenza virus was isolated, a number of research workers have attempted to evaluate the effectiveness of vaccines derived from it. The results of these experiments have been very inconclusive. Some consider that the use of the vaccine has greatly reduced the incidence of cases of respiratory disease, while others think that the attack rate has not been significantly different between controls and vaccinated persons.[1, 2]

Moreover, in the opinion of those who have not merely noted the total incidence of respiratory disease, but also made a distinction between general respiratory disease and true influenza, vaccination with a vaccine of antigenic structure identical with that of the virus responsible for the epidemic has significantly lowered the incidence of influenza in those receiving it.[3-5]

With these studies in mind, we attempted during the course of the winter of 1954-55 to assess in our area the degree of protection conferred by a polyvalent anti-influenza vaccine.§

METHOD OF PREPARATION OF VACCINE

The vaccine was prepared by us in the laboratories of the Institute of Microbiology and Hygiene of the University of Montreal. Preparations included the following steps:

We inoculated each type of influenza virus into the allantoic cavity of chick embryos 11 days old. Embryos inoculated with strains of type A were incubated for 48 hours at 37° C. Those inoculated with a type B were kept at 35° C. for 96 hours. After this period of incubation the allantoic fluid was collected aseptically, and the virus which had multiplied within it was purified and concentrated by centrifugation. After treatment with formol 1 in 4000, the agglutinating power of each monovalent vaccine was adjusted by dilution to 500 units per c.c.

The strains A/PR8/1934, A/FMI/1947, A/Cuppett/1950 and B/Lee/40 were used to prepare vaccine and the latter submitted to control tests in accordance with "Minimum requirements: influenza virus vaccines".[6]

The four monovalent vaccines were mixed in following proportions: PR8, 22.2%; FMI, 22.2%; Cuppett, 22.2%; Lee, 33.3%.

Control solutions were prepared by the same procedure except that the stage of infection of the embryos was omitted. The degree of opalescence of the vaccine was used as a measure of when the moment to dilute the normal allantoic liquid was reached.

VACCINATED GROUPS

Epidemic influenza is usually very unpredictable. It is impossible to predict what group it will affect and what area it will spare. We therefore decided in the winter of 1954-55 to make up four groups of volunteers at random, in an attempt to measure the protection conferred by our vaccine on those vaccinated.

Group 1: At the Psychiatric Hospital

This institution has 6000 patients: 2862 were given the vaccine and 748 the non-virulent liquid (placebo); 1077 served as non-vaccinated controls. In essence this is a very closed community; however, because of the personnel who live outside, the visitors, and those patients who are allowed out, this hospital has frequent and multiple contacts with the population of the city of Montreal.

Group 2: Civil Service, City of Montreal

A group of 558 civil servants were given the vaccine and 476 the placebo fluid; 2466 individuals were used as non-vaccinated controls.

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Group 3: A Montreal Factory

The vaccine was given to 313 workmen and the placebo solution to 277 others.

Group 4:

For a fourth experimental group, we chose a semi-rural area, Montmagny, situated 40 miles down the river from Quebec. The vaccine was administered to 1525 children and 236 adults; 558 children and 195 adults were given injections of placebo.

secure an effective dispersion of the vaccine aerosol into the upper respiratory tract, and in order to maintain the pressure at a constant level in all subjects, the apparatus was connected with an oxygen reservoir. We introduced paper cones with tips cut off into the nostrils; this made it possible to introduce without contamination the ends of glass tubes attached to the vaporizer (Fig. 1). Finally, to make sure that the vaccine penetrated thoroughly, we asked each person to take five deep breaths.

TABLE I.—NUMBER VACCINATED IN EACH GROUP

	One injection of vaccine	*Two injections of vaccine*	*One injection of vaccine; revaccination with aerosol*	*Placebo*	*Not vaccinated*	*Totals*
1. Mental hospital	1114	890	858	748	1077	4687
2. Civil service, City of Montreal	558	—	—	476	2466	3500
3. Montreal factory	313	—	—	277	—	590
4a. Montmagny—children	131	633	761	558	—	2083
4b. Montmagny—adults	—	—	236	195	—	431
	2116	1523	1855	2254	3543	11,291

Study of Table I will show that we divided the four groups into subgroups. The 1st, 2nd and 3rd subgroups were given, either in October or in November, 1 c.c. of vaccine subcutaneously, while the fourth subgroup was given 1 c.c. of the placebo solution, identical in appearance with the real vaccine. It was impossible to distinguish the placebo from the vaccine; the vials of one or the other could be identified only by a number which was unknown both to the administrators and the vaccinated subjects.

In February, persons in the second subgroup were given a second injection of vaccine, while those in the third subgroup were given their booster dose by the nasal route (inhalation). For this purpose we used a Vaponefrin apparatus which discharges droplets 1-2 μ in diameter. In order to

Fig. 1

OBSERVATION FOR RESPIRATORY DISEASE

Group 1 were closely observed by full-time nurses especially chosen for the task. Every morning, the nurses made a round of all wards in order to detect any case of respiratory disease beginning during the preceding 24 hours. They charted any symptoms and complaints and reported these immediately to the physician. The latter then examined these cases on the same day and made a diagnosis. He recorded the results of his examination on a special card and immediately took a specimen of blood and one of throat washings, which were taken to the laboratory on the same day.

The throat washings were frozen at –24° C.; the material to be used for serological tests was maintained at +4° C.

In groups 2, 3 and 4, persons were observed by physicians who usually looked after them. The physician attached to the service of the establishment was to be consulted at the first sign of respiratory disorder. In practice, contact with the physician was slow and three or four days had already elapsed before the physician was able to make a diagnosis. In other words, necessary specimens could be taken only towards the end of the first week.

Nurses responsible for observation of group 4a investigated at home all absences from school. However, there were very few cases of respiratory disease in this observation group.

RESULTS

1. *Vaccination Reaction*

Vaccination led to local reaction in 50% of the adults: redness of skin, mild swelling and local

pain. Of those vaccinated, 35% had mild general reactions, such as headaches and chills, which lasted only for a few hours and did not prevent them from following their usual occupations. General reactions of any severity were observed only in 1% of those vaccinated, and kept them at home for a day. We also noticed that the severity of postvaccinal reactions was directly related to the physical activity of the person. Hence manual workers had much more trouble than clerical workers. On the other hand, there were comparatively few reactions in children, and these were of a benign nature. Table II gives a comparison of

TABLE II.—REACTIONS OBSERVED IN CHILDREN AND IN ADULTS AFTER ADMINISTRATION OF INFLUENZA VACCINE

		Reactions				
			Slight		Strong	
	Number	None	Local	General	Local	General
Adults	377	27%	51%	35%	—	1%
Children	190	69%	27%	25%	—	—

reactions seen in two very different groups: factory workers and school children. Among 8000 subjects given the anti-influenza vaccine or the placebo, no allergic reactions were observed.

2. *Increase in Antibodies after Vaccination*

In order to estimate the increase in antibodies arising after vaccination, we relied on the hæmagglutination inhibition and determined specific antibodies in sera coming from the four following groups:

Unvaccinated subjects	94
Subjects given placebo solution	95
Subjects given one injection only	87
Subjects given two injections	114

This study showed us that the strain B/Lee/40 used in this experiment was a much more powerful antigen, while on the other hand the strain A/Cuppett/50 had little antigenicity; this is in accordance with the facts shown in Table III.

TABLE III.—MEAN TITRE OF ANTIBODIES FOUND TWO WEEKS AFTER REVACCINATION TWO MONTHS AFTER PRIMARY VACCINATION

	Not vaccinated	Placebo	Vaccinated—one injection	Vaccinated—two injections
Number	94	95	87	114
Strain				
PR 8	1/64	1/93	1/732	1/739
LEE	1/62	1/83	1/520	1/1470
FMI	1/74	1/103	1/226	1/240
Cuppett	1/38	1/56	1/100	1/112

It was also shown (Table IV) that revaccination by the intranasal route had no stimulating or booster effect on the production of antibodies.

TABLE IV.—INFLUENCE OF VACCINATION WITH AEROSOL ON THE ANTIBODY LEVEL. MEAN TITRE IN VACCINATED WITH DIFFERENT VACCINES

	Placebo	One injection of vaccine	One injection of vaccine + aerosol two months later
Number	110	70	90
PR 8	1/59	1/235	1/257
LEE	1/96	1/435	1/435
FMI	1/51	1/133	1/152
Cuppett	1/50	1/105	1/115

3. *Influence of Age on the Increase of Antibody Titre*

Antibody production was found to be independent of the person's age. Persons at the age of 60 responded just as well as young subjects to vaccination with influenza virus A. This is shown in Table V, which compares the antibody titre

TABLE V.—INFLUENCE OF AGE ON THE APPEARANCE OF ANTIBODIES AGAINST THE STRAIN PR 8 AS OBSERVED TWO WEEKS AFTER VACCINATION

		Mean titre		
Age	Number	Before vaccination	After vaccination	Increase of antibodies
15 - 19	17	160	567	x 3.5
20 - 24	9	254	806	x 3.2
25 - 29	23	104	653	x 6.2
30 - 34	22	80	413	x 5.2
35 - 39	12	63	214	x 3.4
40 - 44	20	62	309	x 4.9
45 - 49	23	32	200	x 6.2
50 - 54	30	35	292	x 8.3
55 - 59	14	56	284	x 5.1
60 - 64	17	87	244	x 2.8
Totals	183	68	356	x 5.2

before vaccination with titres found two weeks after the latter.

INCIDENCE OF RESPIRATORY ILLNESS IN THE VACCINATED GROUP

Group 1 (Psychiatric Hospital).

Observation of respiratory disorders was possible only in group 1 (Psychiatric Hospital). Nurses assigned to this task visited the wards and took the temperature of all persons with symptoms associated with illness of the respiratory tract.

Fig. 2 takes into account only patients who had a temperature of 100° F. and more. Nurses took throat washings and early specimens of serum (i.e. during the first day of the illness). Ten days later they took a specimen of convalescence serum. The serum specimens were studied for increase in antibodies corresponding to the various viruses presumed to be responsible for the current infection; an attempt was made to isolate the causative virus from throat washings.

Cases of febrile respiratory illnesses were very rare in November, December and January. In

TABLE VI.—INCIDENCE OF RESPIRATORY ILLNESS DURING THE EPIDEMIC OF INFLUENZA

	One injection of vaccine	*Two injections of vaccine*	*One injection of vaccine, revaccination with aerosol*	*Placebo*	*Not vaccinated*
1. Mental hospital	0.9%	1.1%	1.6%	2.5%	4.6%
2. Civil service, City of Montreal	1.4%	——	——	2.5%	5.0%
3. Montreal factory	8.3%	——	——	13.7%	——

February there was a recrudescence of respiratory infections, but only in three cases out of 31 were we able to demonstrate the presence of influenza virus. March was more useful as regards the incidence of respiratory illness. In the majority of cases (78 specimens out of 107 investigated) we succeeded in establishing that the infection was influenza. The antigen structure of the influenza virus isolated showed that it belonged to the strain A/Cuppett/50. Interpretation of radiographs taken in 72 persons in whom the influenza virus had been isolated produced only 17 cases of positive pulmonary findings, as follows: pulmonary congestion, 7; bronchitis, 7; pleuropneumonia, 1; lobar pneumonia, 1; unilateral bronchopneumonia, 1.

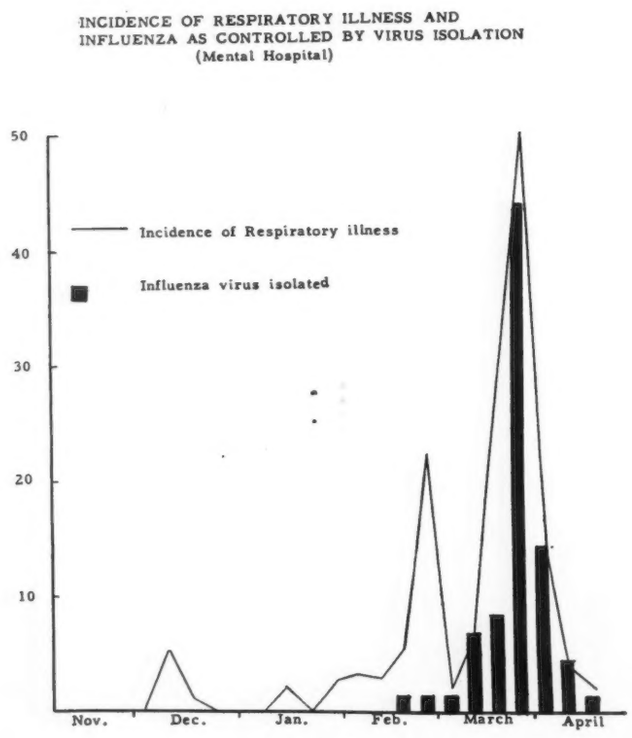

Fig. 2

Comparison of the incidence of influenza in various groups shows that it was 0.9%, 1.6% and 1.1% in the three vaccinated groups, 2.5% in the group given placebo solution, and 4.6% in unvaccinated subjects. Hence the protection conferred by influenza vaccine varied between 40 and 80% according to the group. Administration of a booster dose, either by injection or by intranasal vaporization, appears to have added nothing to the protective effect of the first injection of vaccine.

Group 2 (Civil Service, City of Montreal).

In persons belonging to this group we did not succeed in observing respiratory disease so closely. This was not due to the fact that they neglected to mention their symptoms to the physician, but rather that the latter often took two to three days to respond to their call. Thus in many cases symptoms and disease had disappeared by the time the physician arrived. In such cases the physician made a diagnosis of "influenza" on the strength of the patient's statement. Naturally in such cases we were unable to take specimens (blood or throat washings). However, during this period many of the civil servants in the city were absent from work because of respiratory infection (Fig. 3); in fact, during the month of March, when the influenza epidemic was raging, absenteeism for respiratory illness doubled among municipal civil servants.

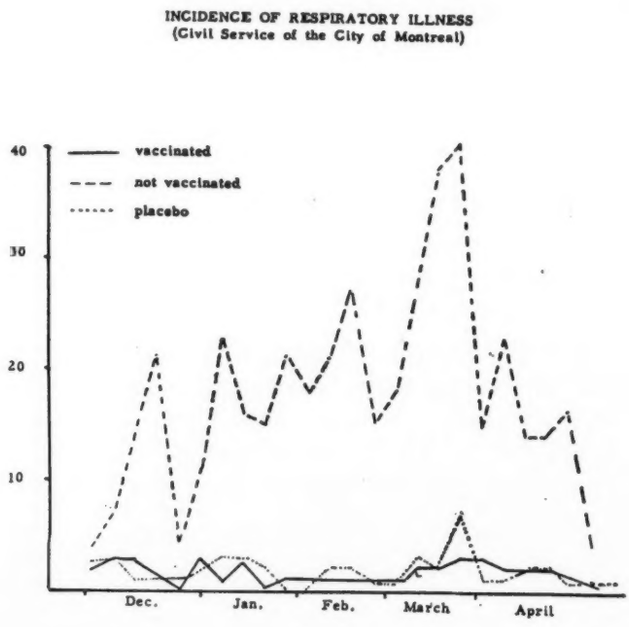

Fig. 3

Thus it is logical to conclude that the influenza epidemic had attacked groups 1 and 2 at this time. Moreover, a comparative study of attack rates among the various groups of civil servants reveals a level of protection varying from 40 to 72% in the subjects who were vaccinated.

Group 3 (Montreal Factory).

This was the group most affected by respiratory illness. Of those vaccinated in this group 38%

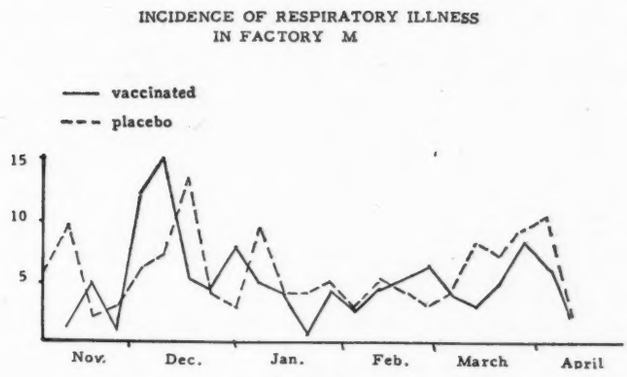

Fig. 4

(120 out of 313) were absent from work because of respiratory illness, against 48% (134 out of 277) of their unvaccinated companions who had been given the placebo.

If we compare the incidence of respiratory illness during March—the time when the influenza epidemic was present in Montreal—we find that 8.3% of the vaccinated persons had a respiratory illness as against 13.7% of the persons given the placebo. Hence vaccination conferred protection of the order of 40% in this case.

Group 4 (Montmagny).

There was no respiratory illness in Montmagny in the winter of 1954-55, and the laboratory also appeared to confirm the entire absence of influenza virus from this locality during the relevant period.

DISCUSSION

Influenza is a local infection of the respiratory tract. It is characterized by necrotic degeneration of ciliated epithelium which lines the tract.[7] The influenza virus multiplies in the superficial cell layer of the respiratory mucosa.

There is a close parallelism between the subject's resistance to influenza and the titre of antibodies present in the secretions of the respiratory mucosa. It is therefore possible to increase a person's resistance to influenza by increasing this local immunity. Fazekas de St-Groth,[8] working with mice, showed that nasal instillation of anti-influenza vaccine, done either at the same time as or after the intraperitoneal injection of a dose of the same vaccine, made the animal 100 times more resistant to experimental influenza infection. It is also known that penetration into the air channels and fixation on their lining mucosa is better when an aerosol is used than when nasal instillation alone is relied upon. Fixation of droplets present in an aerosol depends on their diameter; the best results have been obtained with particles of size 0.8 to 1μ.[9]

Knowledge of these facts led us to administer the second or booster dose of vaccine to the subjects participating in our experiments by nebulization. For this purpose we used the De Vilbiss vaporizer, which produces particles of 1μ. diameter. In our experiments this intranasal nebulization of vaccine did not give the expected results. It gave absolutely no increase in resistance of vaccinated subjects. Zhdanov[10, 11] also noted that intranasal administration of virus inactivated by formol did not increase resistance to influenza infections. On the other hand, he obtained good results by using a living virus.

During the winter of 1954-55 respiratory illness occurred in all the groups observed by us. The attack rate varied from one group to the next. In the factory group out of 313 subjects vaccinated 120 (38%) had respiratory illness, whereas in 277 controls unvaccinated there were 134 illnesses, i.e. 48% (Fig. 2). The municipal civil servants in Montreal had an absence rate of 7.9% and 13% (Fig. 4).

In March there was a recrudescence of respiratory infections in the three Montreal groups under our observation; in fact, it was during this period that we isolated the influenza virus in 70% of cases. In the beginning of the epidemic we isolated it only in 27% of cases, whereas towards the end the percentage of positive results reached 96%. It is possible that this influenza epidemic was preceded in February by an epidemic caused by another virus. Our results are similar to those of Hilleman and his colleagues,[12] who reported that an epidemic of RI-67 infection preceded the influenza epidemic which they studied.

We were entirely satisfied with the antigenic qualities of the vaccine we used. There was an increase in antibody titre against the four component strains. The strain B/Lee/40 proved the most active; the strain A/Cuppett/50 was the weakest.

Using a vaccine of identical composition, Buchner, Reid and Dempster[13] observed a comparable increase in antibodies in vaccinated subjects.

The attack rate for respiratory illness was nevertheless different among subjects receiving the placebo and unvaccinated subjects. At the Hôpital St-Jean-de-Dieu influenza affected 2.5% of the subjects given the placebo, whereas the attack rate was 4.6% for those given nothing. This difference may be explained by the fact that those who received the placebo were in the same wards as the vaccinated. They must therefore have benefited from the protection furnished to the latter. The same explanation holds good for the group made up of civil servants of the City of Montreal. Vaccinated subjects and those given the placebo solution were recruited from among firemen attached to the same fire halls, whereas the control unvaccinated group was composed of men belonging to other fire halls. In this group we also arrived at the conclusion that vaccinated and less affected subjects protected to a certain extent their placebo-inoculated companions; in fact, there was 50% less respiratory illness among them than among firemen from other fire halls.

SUMMARY

During the winter of 1954-55 we attempted to evaluate in human subjects the effectiveness of a quadrivalent anti-influenza vaccine.

An epidemic of mild influenza affected Montreal in March 1955, and its origin was traced to a virus of antigenic structure identical with that of virus A/Cuppett/50.

The quadrivalent vaccine given in our study led to an appreciable production of antibodies; their titre was quadrupled for strains A/PR8/34 and B/Lee/40, the response being much weaker with strains A/FMI/47 and A/Cuppett/50.

This quadrivalent vaccine conferred a protection against clinical influenza varying between 40% and 80% according to the group.

Our thanks are due to Dr. G. Charette, epidemiologist of the City of Montreal, and Dr. A. Dumas, director of the Montmagny Health Unit, for their help in this study.

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RÉSUMÉ

Au cours de l'hiver 1954-1955 nous avons tenté d'évaluer chez l'homme l'efficacité d'un vaccin quadrivalent.

Le vaccin a été préparé à l'Institut de Microbiologie et d'Hygiène de l'Université de Montréal à partir des souches suivantes: A/PR8/1934, B/Lee/1940, A/FMI/1947 et A/Cuppett/1950. La vaccination a été faite 1) à l'Hôpital pour les maladies mentales, 2) dans le service civil de la ville de Montréal, 3) dans une usine de Montréal et 4) dans une localité semi-rurale sise 40 milles en aval de Québec. Dans tous ces groupes les sujets ont été divisés dans les sous-groupes suivants: 1er sous-groupe ayant reçu une injection de vaccin, 2e ayant reçu deux injections de vaccin, 3e ayant reçu une injection de vaccin avec la vaccination de rappel par aérosol, 4e ayant reçu une injection de placebo. Dans le groupe 1 et 2 nous avons observé aussi des sujets non vaccinés qui habitaient dans les mêmes conditions que les sujets vaccinés. Au total 5494 sujets ont reçu le vaccin antigrippal, 2254 ont reçu une injection de placebo et 3543 ont servi comme témoins non vaccinés.

Le vaccin quadrivalent employé en cette circonstance donna lieu à une production d'anticorps appréciable, leur taux quadruplé pour les souches A/PR8/1934 et B/Lee/1940, la réponse restant beaucoup plus faible avec les souches A/FMI/1947 et A/Cuppett/1950.

Une épidémie de grippe bénigne a sévi à Montréal en mars 1955 et on a pu en relier l'étiologie à un virus de structure antigénique identique au virus A/Cuppett/1950.

En comparant la fréquence de la grippe chez les sujets en observation à l'hôpital des maladies mentales on remarque qu'elle a été de 0.9%, 1.1% et 1.6% dans les trois sous-groupes de vaccinés, de 2.5% dans le groupe ayant reçu la solution placebo et de 4.6% chez les sujets non vaccinés.

Dans le deuxième groupe (Service civil de la ville de Montréal) nous avons observé que 1.4% des vaccinés, 2.5% des sujets ayant reçu une injection de placebo et 5% des témoins non vaccinés se sont absentés de leur travail à cause des maladies respiratoires.

Dans l'usine M., où le taux des maladies respiratoires a été très élevé, pendant l'épidémie de la grippe nous avons observé 8.3% des maladies respiratoires parmi les vaccinés et 13.7% parmi ceux ayant reçu le placebo.

Ces résultats permettent de conclure que le vaccin quadrivalent donna contre l'influenza clinique une protection variant de 40 à 80% selon les groupes.

SUBARACHNOID HÆMORRHAGE, 1951-1958: 108 Cases*

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OUR FIRM CONVICTION of the practical inefficacy of emergency operation for subarachnoid hæmorrhage was the reason which dictated our method of treatment.

As our treatment has been systematically the same for all patients in this group, we think that the present analysis may be of value in showing whether our final results can be compared with those from other methods of treatment, and whether this treatment has been better or worse for our patients.

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Presented at the Meeting of the Quebec Division of the C.M.A., Ste-Adèle, Que., May 2, 1958.

TREATMENT

1. No intracranial operation is performed before at least 15 days after the hæmorrhage. Angioma and intracerebral hæmatoma are the only indications for such operation.

2. On admission, whatever his condition, the patient is put on a "uniform medical" treatment until his physical and neurological conditions have improved sufficiently to allow arteriography to be done with fair security.

3. A lumbar puncture, if indicated, is performed on admission, and only a few drops of fluid are withdrawn — enough to confirm the diagnosis.

4. The most absolute rest is imposed. The least physical efforts are avoided by the patient, who is fed for at least one week with adequate feedings and fluids. As soon as possible the exact problem is explained to the patient; the purpose of our treatment is also explained to him in order to obtain his full co-operation and to reduce his anxiety.

Agitation and anxiety state determine the doses of sedative. Subsequent lumbar punctures are postponed as long as possible after the time of hæmorrhage; persistence of or increase in fever, unconsciousness, rigidity of the neck or a state of agitation are their sole indications.

5. Bilateral arteriography under general anæsthesia is performed percutaneously as soon as the physical condition will permit this procedure with security. As we all know that the most dangerous period as regards recurrence of hæmorrhage is between the 7th and 14th days, we usually perform arteriography before that period.

On four occasions, because patients were admitted for a second hæmorrhage or were convalescent after their hæmorrhage, we performed arteriography and installed the clip 24 to 36 hours after admission.

6. After bilateral arteriography:

A. When only one aneurysm was found, whatever its location, except on the basilar or cerebellar artery, a Silverstone clip was applied to the common carotid artery of the proper side and progressively closed in five or seven days.

B. When an angioma was the lesion and was surgically accessible, it was removed by intracranial operation when the physical condition suggested that this could be done with a fair chance of success.

C. When an intracerebral hæmatoma was found, the treatment was the same as for angioma.

D. When two or more aneurysms were found or the arteriograms were negative, patients were kept on medical treatment and were rarely discharged before four or five weeks.

7. Vertebral arteriography was omitted because, knowing that no surgical treatment would be advisable, we did not feel that we should impose this test on a patient just for a diagnostic reason, although we knew that an angioma of the cerebellum might on very rare occasions be the cause of the hæmorrhage.

Summary of Treatment

1. Strict and uniform medical treatment for at least eight days after the hæmorrhage.
2. Bilateral arteriography under general anæsthesia.
3. All single aneurysms treated only by clipping the common carotid artery.
4. Intracranial operations only for angioma or intracerebral hæmatoma.
5. No direct attack on the aneurysms.

ANALYSIS OF OUR GROUP

1. *Arteriograms (Table I); Pathology (Table II); Etiology (Table III)*

The percentages of arteriograms made, of pathological lesions found and of cases of known and unknown etiologies, are about the same as those in reports from other services.

TABLE I.—ARTERIOGRAMS

			87 = 80.5%
Positive	39	Aneurysms	37
		Angioma	1
		Hæmatoma	1
Negative	48		

TABLE II.—PATHOLOGY

			47 = 43.5%
Aneurysms	42	Arteriography	36
		Autopsy	6
Angiomas	2	Arteriography	1
		Autopsy	1
Hæmatomas	3	Arteriography	1
		Autopsy	2

Although our cases of subarachnoid hæmorrhage due to arterial hypertension were fairly few, our percentage (80.5%) of cases with arteriograms, our numerous postmortem examinations, our number of cases in which lesions were found, and those of unknown etiology are not different from others.

TABLE III.—ETIOLOGY
ARTERIOGRAPHY OR AUTOPSY

Authors	*Total*	*Known*	*%*	*Not known*	*%*
Newcastle	312	84	26.9%	228	73.1%
Odom	316	173	54.7%	143	45.3%
Dekaban and McEachern	100	44	44.0%	56	56.0%
Sirois	108	47	43.5%	61	56.5%

2. *Mortality*

We tried to compare our mortality rate with rates from other services, and to relate it to the time of hæmorrhage, the time of admission and hæmorrhage and the various treatments.

TABLE IV.—MORTALITY RATE OF SUBARACHNOID HÆMORRHAGE
IN COMPARISON WITH OTHER SERVICES

Authors		*No. of cases*	*Deaths*	*Percentage*
Taylor, Whitfield		81	51	63%
Sands	1941	120	41	34%
Fetter	1943	68	24	39%
Magee	1943	150	84	56%
Sahs, Keil	1943	64	18	28%
Wolf	1945	46	15	33%
Hamby	1948	130	67	51%
Hyland	1950	191	100	53%
Ask, Wymark, Ingvar	1952	138	38	28%
Dekaban, McEachern	1952	87	32	37%
Wolfe	1953	93	52	56%
Newcastle Series	1956	312	140	45%
Sirois *et al*	1958	108	24	22.3%

A. *Table IV:* On comparison with figures from other services (not only those published by Walton but also many others), we were rather surprised to find that our percentage, 22.3%, for general mortality is much lower than the average.

TABLE V.—MORTALITY IN COMPARISON WITH TIME OF HÆMORRHAGE

Admission	*No. cases*	*Mortality*	*Living*
Less than 24 hours after hæmorrhage...	24	15=62.5%	9=37.5%
More than 24 hours after hæmorrhage...	84	9=10.7%	75=89.2%

B. *Table V:* If we take the time of the hæmorrhage and the time of admission in relation to mortality, we see that our number of cases, 24 or 22.2%, admitted less than 24 hours after hæmorrhage is low, but that the number surviving, 9 or 37.5%, in that category is somewhat larger than in most services. So is our percentage surviving, 89.2%, of the 84 patients admitted later than 24 hours after the time of the hæmorrhage.

TABLE VI.—MORTALITY IN COMPARISON WITH TIME OF ADMISSION AND TREATMENT

Treatments	*No. of cases*	*Dead* *Less than 24 hrs. after admission*	*Dead* *24 hours after admission*
Medical.....	78	12=15.3%	8=10.2%
Medical and surgical	30	4=13.3%	0
Total.....	108	16=14.8%	8= 7.4%

C. *Table VI:* The mortality rate, in relation to the time of admission and the varieties of treatment applied, is very satisfying and we think that few services have had a rate of mortality as low as we have obtained with our treatment.

TABLE VIII.—RESULTS TO DATE

Cured.....	71	65.7%	
Dead.....	24	22.3%	Morbidity=3.5%
Sequelæ.....	13=12.0%		Unable to work..... 3 Lighter work..... 2 Usual work..... 8

Mortality—22.3%:

Our general mortality rate of 22.3% is the lowest in Table IV and also the lowest in any analysis of a group of at least 100 cases which we have seen in the literature. It is in fact better than we could have hoped for at the beginning of this treatment.

Morbidity—3.5%:

Thirteen patients (12%) had some general sequel, but two have returned to lighter work than before their hæmorrhage and 8 were able to resume their usual work. Only 3 out of 84 survivors (3.5%) were left with a complete disability.

These two figures show better results than anyone can hope for with intracranial surgical treatment, especially as regards morbidity.

COMMENTS

Unknown Etiology:

It is quite disturbing to note that so many cases of subarachnoid hæmorrhage remain of unknown etiology. This has been observed everywhere and is mentioned in almost all papers;

TABLE VII.—MORTALITY IN COMPARISON WITH TREATMENT

Treatment	*Rowley, 157* *No. of cases*	*Dead*	*%*	*Sirois, 108* *No. of cases*	*Dead*	*%*
Medical.....	145	69	47.5%	78	20	25.6%
Ligature of common carotid.....	6	2	33.3%	28	2	7.1%
Ligature of internal carotid.....	1	0	0	0	0	0
Intracerebral.....	5	3	60.0%	2	2	100.0%
Totals.....	157	74	47.2%	108	24	22.2%

D. *Table VII:* The report of Rowley *et al.* (St. Louis, Missouri) was chosen to establish a comparison between mortality rate and variety of treatment, because of the great similarity of the two services, for example, 7.8% of Rowley's cases and 2.1% of ours had intracranial operations. For the past seven years, we think that these are the lowest figures for most services for treatment by intracranial surgery. Comparison of these figures with others speaks for itself.

Results (Table VIII):

This table contains the principal statistics from which the value of our treatment can be judged. Indeed, the purpose of any treatment is directed to two goals: to prevent mortality and to cause the least possible morbidity.

nevertheless one has the impression that this group is forgotten. Lack of interest in this group may be due to the well-known fact that they are the luckiest of all as far as prognosis is concerned. We have to admit that we are still in the dark as to the cause of their hæmorrhage and our complete disinterestedness in finding it out.

This group is more numerous than the other, as observed by everyone. This should make us bitterly disappointed at our lack of knowledge, and stimulate everyone to direct our efforts towards the understanding of these "unknown etiologies". Who knows but that our present concepts of treatment would not then completely change?

Mortality:

The general mortality rate from subarachnoid hæmorrhage is much too high. No doubt it is a

consequence of the large number of patients who die less than 24 hours after their hæmorrhage. But the rate for the other group, namely those who have survived the critical period of 24 to 36 hours after hæmorrhage, also remains too high. Two remarks seem appropriate.

First: Most of the patients who die within 24 to 36 hours of their hæmorrhage have become deeply comatose or decerebrate, or have shown signs of cerebral trunk impairment so quickly, that we doubt whether we can accomplish anything for them with any kind of treatment.

We think that these cases should be excluded from the statistics, and all of our research and studies be limited to the second group, until a proper method of treatment, reducing mortality and morbidity to a decent minimum, is accepted by most neurological and neurosurgical groups.

It would be possible then, as suggested by Sir Geoffrey Jefferson in Toronto at the 1955 Annual Meeting of the Canadian Neurological Society, to undertake an adequate review from all sources. Indeed analysis of these cases, all studied on the same basis, would permit an exact evaluation of the varieties of treatments used, and reveal the one which has accomplished the best results as regards mortality and morbidity rates.

Second: The high mortality rates in the second group of patients, the morbidity among survivors and the great variety of treatment given are unquestionable proof that treatment at present is far from satisfactory.

This supports the suggestion of Sir Geoffrey Jefferson, and should stimulate everyone to help with the formation of a group which will undertake the task of clarifying this question.

Morbidity:

As mentioned before, morbidity is a good criterion for the assessment of treatment. In published statistics, morbidity too often seems to be a second thought and at times is not even mentioned.

The satisfaction for a surgeon in having a patient come through a very laborious intracranial removal, packing or tying of an aneurysm may be stimulating, but one often wonders how it is appreciated by a patient who will be left with a partial or a complete disability for the rest of his life, or will have to depend upon public charities for his needs.

Morbidity should be on the same basis as mortality when the value of any treatment is judged, and especially so when treatment is directed at the most essential human organ. Between medical and surgical treatment, which would we all choose if we were to be the patient?

Treatment:

If good results are to be expected with our treatment, it is imperative to maintain very strictly the following rules:

1. *Absolute rest,* meaning that any physical movement or effort by the patient should be limited to the essentials; the patient must be kept very quiet if unconscious, relaxed and confident if conscious. He is not to be removed from his room.

These first rules are observed very strictly until the physical condition, rather than the neurological condition, has so improved as to permit diagnostic procedures to be safely undertaken. We do not allow these rules to be broken even if there is a recurrence of bleeding, if the general physical condition is not judged satisfactory. The period of absolute rest has varied from eight to twenty days.

2. The *diagnostic procedures,* including routine radiography of the head, are begun then. Bilateral arteriography is always performed under general anæsthesia because it eliminates any cause of anxiety, which we think is important especially when the procedure offers difficulties.

3. Intracranial surgery is reserved for cases with an angioma or an intracerebral hæmatoma. Progressive occlusion with a Silverstone clip is the sole surgical procedure used when an aneurysm is found, whatever its localization.

An analysis of all our cases of progressive carotid occlusion by a Silverstone clip is in preparation.

CONCLUSIONS

Our low mortality rate—10.7% of 84 patients who had survived the 24 to 36 hours after their hæmorrhage—and our low morbidity rate, 3.5%, are the lowest we have found in the literature; this seems to indicate: (1) That our method of treatment has responded to our wishes. (2) That the fewer manipulations are done to these patients during the first 8 to 10 days the better their chances are. (3) That it is possible that clipping of the carotid artery will remain the only surgical procedure of choice for patients with intracranial supratentorial aneurysm.

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RÉSUMÉ

Les auteurs de cet article font part des résultats obtenus dans le traitement d'une série des cas d'hémorragie sous-arachnoidienne d'après un traitement fondé sur: 1) un repos complet au lit pendant une période variant de huit à vingt jours; 2) l'artériographie bilatérale sous anesthésie générale; 3) une intervention réservée uniquement aux cas où les procédés diagnostiques ont révélé la présence d'angiomes ou d'hématomes intracérébraux.

Dans une série de 84 malades ayant survécu de 24 à 36 heures après l'hémorragie initiale le taux de mortalité fut de 10.7% et le taux de morbidité de 3.5%. Ces chiffres se situent parmi les plus bas de tous ceux qui ont été rapportés à date. Les auteurs semblent croire que l'occlusion de l'artère carotide par des agraffes pourrait bien demeurer le seul procédé chirurgical satisfaisant dans le traitement des malades atteints d'anévrisme des vaisseaux de la loge cérébrale.

HÆMORRHAGIC EFFECT OF ACTH WITH ANTICOAGULANTS*

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IN THE experimental development of anticoagulants, it was early remarked that hæmorrhage was hardly ever observed in normal animals. This was true even with values of the prothrombin time much beyond any encountered clinically. In view of the not too uncommon complication of hæmorrhage with the clinical use of anticoagulants, this suggests that some important factor or factors in the production of hæmorrhage have been overlooked. Recent studies[1] in the laboratory at Saskatoon have demonstrated that stress constitutes such a hæmorrhagic factor. When rabbits receiving dicoumarol, etc., are exposed to such stress as frost-bite, insulin convulsions, and injection of 10% sodium chloride intraperitoneally, 50% will die between 60 and 72 hours later. At postmortem, hæmorrhage can be demonstrated in many animals. This may be subcutaneous, or into the pleural or other cavities, externally or at other sites. This phenomenon has been termed hæmorrhagic death and can be produced by various combinations of treatments. In the present experiments, the effect of combining treatment by pituitary hormones and corticosteroids with treatment by dicoumarol has been studied. Two cases are presented which appear to illustrate the corresponding clinical problem.

Methods‡

Rabbits from the normal colony stock of 2-4 kg. body weight were used. Dicoumarol was given in a single oral dose of 5 mg./kg.; phenylindanedione as an initial dose of 100 mg./kg. followed by 25 mg./kg. three times a day for 5 days; ACTH, somatotrophin, cortisone and desoxycorticosterone were administered intramuscularly as a single dose of 5 mg./kg. at the same time as the first dose of anticoagulant. In one experiment the ACTH was repeated daily for five days. Prothrombin times were carried out by the Quick technique using commercial rabbit brain thromboplastin.

RESULTS

Hæmorrhagic death in rabbits.—Forty-one rabbits were treated with 5 mg./kg. of dicoumarol and the prothrombin time was followed. One of these rabbits died from hæmorrhage on the fifth day. Blood from the intestine was found in the cage, but lungs and other viscera appeared normal. After the prothrombin time returned to normal and after a further rest period of several weeks, the treatment with dicoumarol was repeated and at the same time ACTH was injected. Ten of these animals died. Fig. 1 shows the lungs of one of these animals compared with those of a normal rabbit. Marked congestion and œdema can be observed. Tissues from three other rabbits dying with hæmorrhage are shown in Figs. 2 and 3.

TABLE I.—INCIDENCE OF HÆMORRHAGIC DEATH IN RABBITS RECEIVING ANTICOAGULANTS AND ACTH

Dicoumarol alone	1/41
" + ACTH	10/40
" + somatotrophin	1/11
" + desoxycorticosterone	0/7
" + cortisone	0/9
Phenylindanedione alone	1/7
P.I.D. + ACTH	4/6
Dicoumarol + ACTH repeated daily	0/13

Of the animals receiving dicoumarol and ACTH, one animal died within 24 hours with hæmorrhage in the kidneys and lungs; one died in 48 hours with hæmorrhage in the kidneys, and one in 72 hours, again with hæmorrhage in the kidneys and lungs. Three animals died on the sixth day. One showed the typical picture of hæmorrhage and congestion in the lungs. One showed slight bleeding only from the nose and ears but post mortem all the organs were quite pale, indicating that extensive hæmorrhage had occurred. The other

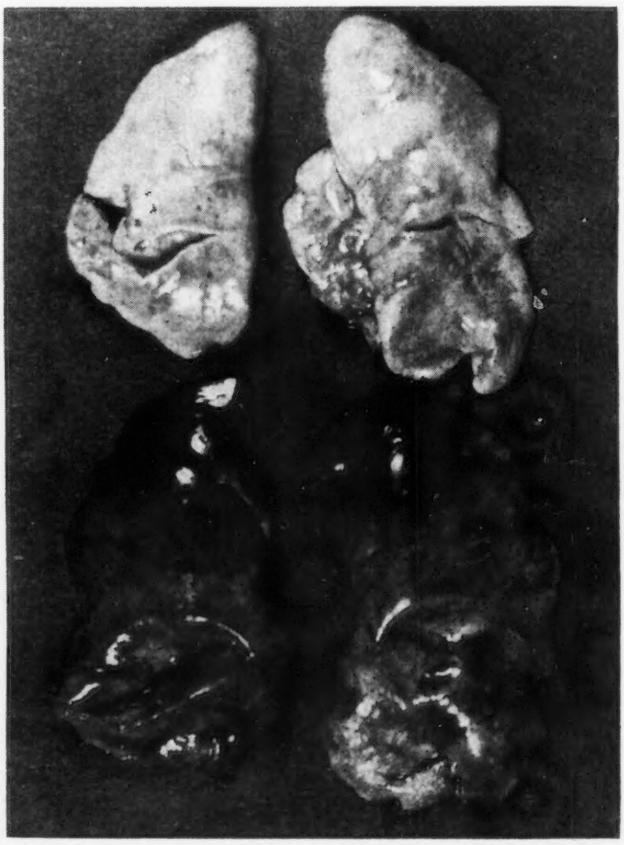

Fig. 1.—Lungs from normal, control rabbit above; lungs from rabbit dying of hæmorrhage after dicoumarol and ACTH below. Marked congestion and œdema.

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‡We are indebted to Chas. E. Frosst & Co. for the phenylindanedione, to Abbott Laboratories Ltd. for the dicoumarol and to the National Research Council of Canada for ACTH. The growth hormone used in this work was a gift from the Endocrinology Study Section, National Institutes of Health, and was a highly purified bovine preparation (NIH-BGH-1).

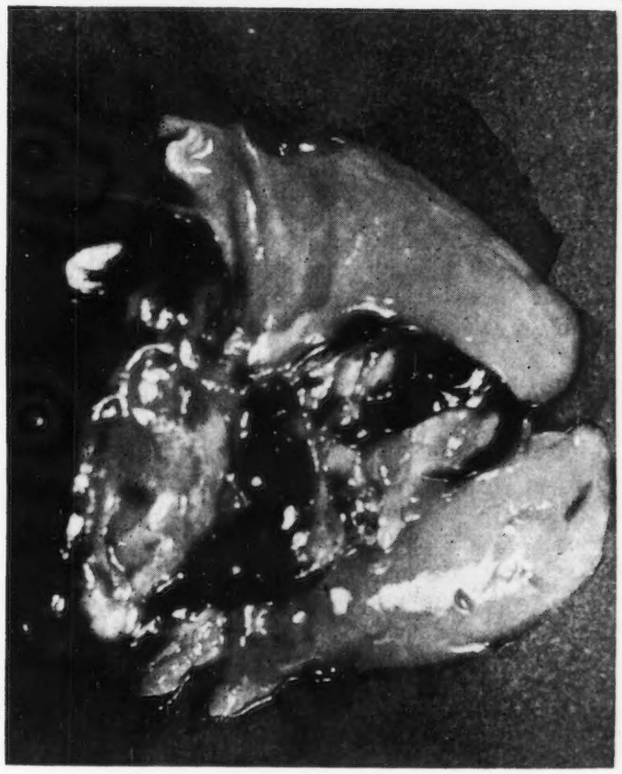

Fig. 2.—Lungs and heart from rabbit dying of hæmorrhage after dicoumarol and ACTH. Death on seventh day. Extensive hæmopericardium and congestion.

showed intestinal hæmorrhage. Three rabbits died on the seventh day. One showed hæmorrhage and congestion in the lungs and kidneys, while the third showed an extensive hæmopericardium. One animal died on the eighth day and showed patchy hæmorrhage in the lungs, hæmorrhagic areas in the intestine and blood in the peritoneum. Another animal showed bleeding from the mouth and nose on the third day but survived. Only one animal died of hæmorrhage on receiving dicoumarol and somatotrophin and no animals died after treatment with cortisone or desoxycorticosterone with dicoumarol. The animal receiving somatotrophin died on the third day with intestinal and peritoneal hæmorrhages.

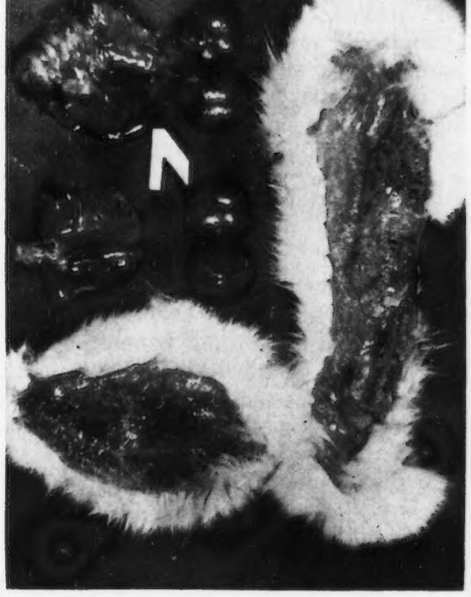

Fig. 3.—Two rabbits dying 24 hours after ACTH and P.I.D. Extensive subcutaneous hæmorrhage. Congestion of lungs. Ecchymotic spots on surface of kidneys.

A small series of animals was tested with phenylindomedione (P.I.D.) and ACTH. Two died 24 hours after ACTH with hæmorrhages in lungs, kidneys, uterus and subcutaneous tissue. One rabbit was found dead on the fifth day with hæmorrhage in the uterus and diffuse hæmorrhage in the left lung. One rabbit was found dead on the eighth day with blood in the urine and patchy hæmorrhage in the lungs. The very high incidence of hæmorrhage and death following ACTH in animals receiving P.I.D. is striking. Actually hæmorrhage from this anticoagulant alone is quite rare in rabbits. When it occurs, it is due to the trauma to the mouth involved in giving the drug in capsule form three times a day, as was the case with the single animal which died after P.I.D. alone. This animal died on the sixth day after bleeding from the jaws and ears from the second day. No lesions were found in the organs but these were very pale.

Finally a small series of rabbits received dicoumarol and 5 mg./kg. of ACTH daily for five days, starting with the administration of dicoumarol. No deaths occurred in this series.

Prothrombin time in rabbits.—Prothrombin times were determined on the animals before the administration of dicoumarol and one, three and five days thereafter. As has been reported by Link[2] and further studied by Jaques *et al.*,[3] rabbits show the phenomenon of resistance, so that rabbits can be divided into reactive and non-reactive rabbits (those showing an increase in prothrombin time and those showing no increase in prothrombin time after dicoumarol). On the basis of the results obtained, animals were sorted out into reactors and non-reactors. The mean prothrombin times are reported in Fig. 4 for all the animals. With the very wide spread in prothrombin times resulting after the administration of dicoumarol, arithmetic means of the values themselves have not a great deal of meaning. It has been pointed out by Mogenson, Fisher and Jaques[4] that if log values of the prothrombin times are taken this gives an approximately normal frequency distribution curve and therefore some meaning to the ordinary statistical procedures such as standard deviation. The prothrombin times were therefore transposed to corresponding logarithmic values, and the mean and standard error calculated for each set of data. Examination of Fig. 4 suggests that ACTH was successful in converting non-reactor rabbits to reactor rabbits. There is a suggestion, though, that the prothrombin time in the reactor rabbits returns to normal more rapidly after ACTH and the prothrombin time was not sustained as long in the ACTH-treated non-reactor rabbits.

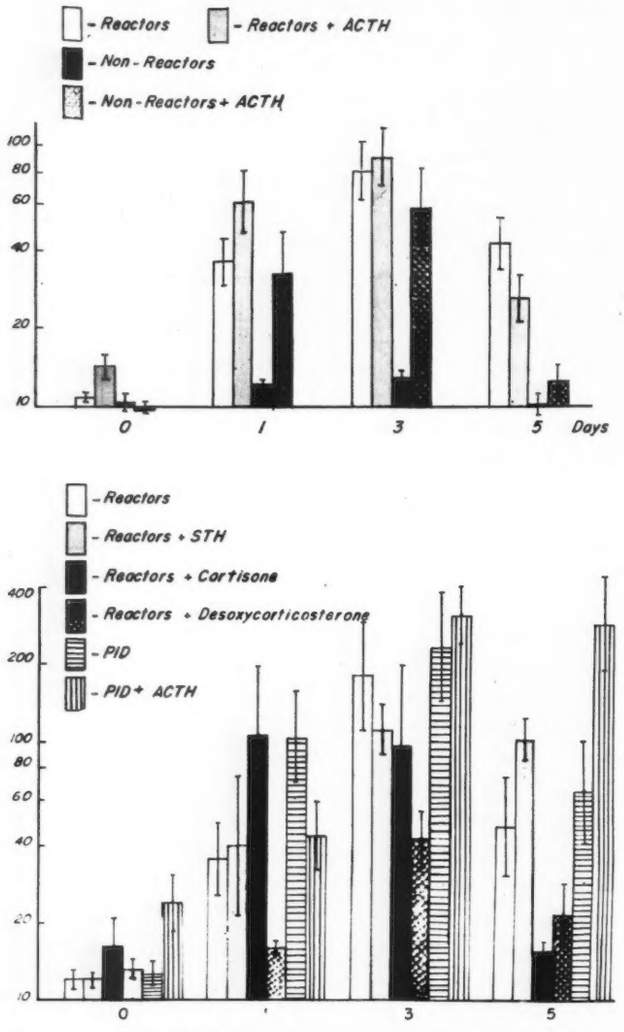

Fig. 4.—Prothrombin time response of rabbits to dicoumarol when treated with ACTH, etc. Anticoagulant and hormone both given on Day O, and prothrombin times determined as shown. Prothrombin times plotted as the mean of the log values of prothrombin time in seconds with standard error. P values were calculated comparing mean values of prothrombin time for the same rabbits receiving dicoumarol with and without the hormone, not against the mean value for all reactor animals shown in figure.

The t test was applied to determine the significance of differences in the mean values. In reactor rabbits, there was no significant difference in the mean prothrombin time on days following dicoumarol, with and without ACTH. On the other hand, there was a marked increase in the prothrombin time of the non-reactor rabbits receiving dicoumarol and ACTH. This, of course, is highly significant when compared with the normal values seen for the same animals with dicoumarol alone on the first and third day after dicoumarol; in fact, the mean values are the same as for reactor rabbits on dicoumarol alone. There is, however, one difference. The mean prothrombin time on the fifth day after dicoumarol is not significantly greater than normal, and hence much less than for reactor rabbits five days after dicoumarol. Presumably this is due to disappearance of the injected ACTH. To test this, another series of animals were given 5 mg./kg. of ACTH each day for five days. Only three proved to be non-reactors. These last three were converted to reactors by ACTH, but the continued daily administration of ACTH following dicoumarol did not maintain the prothrombin times at high values.

Somatotrophin, cortisone and desoxycorticosterone also did not significantly affect the increased prothrombin time induced by dicoumarol in reactor rabbits. The apparent difference seen in the graph with desoxycorticosterone is due to the fact that the group of reactor rabbits used did not give as long prothrombin times with dicoumarol alone as the other groups used. Values were therefore compared for the same animals with and without DOCA. There was no significant difference. Unfortunately, non-reactor rabbits were not available in adequate numbers for this experiment. Desoxycorticosterone and somatotrophin were each given to one non-reactor rabbit without any increase in prothrombin time being observed with dicouma One non-reactor rabbit received cortisone and then showed an increase in prothrombin time ($>$ 480 sec. on the first and third days and 15.6 sec. on the fifth day), while a second non-reactor rabbit gave the same prothrombin times after dicoumarol and cortisone as after dicoumarol alone. We do not find rabbits which are non-reactors to P.I.D. The injection of ACTH did not change the prothrombin time response to P.I.D.

Case Reports

The association of hæmorrhage with the combined treatment of animals with dicoumarol and ACTH suggests the need for examining this as a possible source of clinical bleeding. Two cases which occurred in the Medical Clinic A, University of Liège, are reported.

1. D . . . Jeanne, suffering from rheumatoid arthritis for more than 12 years, was admitted to the medical ward on August 1, 1952, with phlebitis of the right leg with œdema. She was treated with ethyl biscoumacetate (Tromexan) and penicillin for three weeks without any other therapy. The prothrombin level was continuously controlled at between 25 and 45% without any sign of hæmorrhage on one tablet of Tromexan a day. By August 20 the phlebitis was ameliorated but her rheumatoid arthritis was very painful, with increased sedimentation rate and high temperature. ACTH was administered intravenously (10 mg. in 500 ml. of 5% dextrose twice daily) and Tromexan and penicillin were continued. After three days of this treatment with ACTH associated with Tromexan and penicillin, frank hæmorrhage was observed in the stool, the benzidine test for blood in the urine was positive and microscopic examination revealed red cells. The patient was anæmic (Hb. 6.5 g. %; 10.5 g. % before treatment with ACTH). Both drugs were discontinued and 1500 ml. of blood was transfused over a period of five days. The patient recovered from the effects of this hæmorrhage. A barium series proved to be normal.

2. L . . . Marie, a married woman, 61 years old, was admitted to the Liège University Hospital on

March 3, 1953. She was suffering from subacute lupus erythematosus with skin manifestations on the face, the hands, the feet and the neck, and also with pleural effusions, bronchopneumonia in the right lower lobe, albuminuria and fever. There was an increased sedimentation rate (56 mm./1st hour) and raised γ-globulin level. On March 5, administration of penicillin and 40 units a day of Cortrophin-Zinc (long-acting delayed-action ACTH) was begun. On March 8 the temperature was normal and the sedimentation rate decreased to 27 mm./1st hour. On March 10 some ecchymotic lesions appeared on the arms and the legs. The next day new ecchymotic lesions appeared on the trunk and the limbs, accompanied by gross melæna with severe anæmia. The fever reappeared, and in spite of transfusion the melæna and anæmia increased (Hb. 4 g. %) with an increase in the hæmorrhagic lesions over the whole body. The number of platelets was 175,000/c.mm., the prothrombin level 42% and the mean bleeding time 4 min. 24 sec. The patient died March 13/14.

Discussion

As reported in previous papers, mortality due to hæmorrhage is quite small with these doses of anticoagulants in rabbits. However, when ACTH was given with dicoumarol or phenylindanedione, a considerable number of animals died of hæmorrhage, the pathological picture being similar to that previously observed in animals receiving these anticoagulants and subjected to stress. The first case reported is remarkably similar to our animal experiments. The patient was maintained on Tromexan for three weeks without any sign of hæmorrhage. When she was given ACTH, severe hæmorrhage developed in three days, as in the rabbits. Withdrawal of drugs and transfusion saved the patient. The second patient illustrates how severe hæmorrhage can be with ACTH. Here anticoagulants had not been administered but the patient had a correspondingly low prothrombin time, presumably due to the accompanying clinical pathology affecting the liver. The administration of ACTH then precipitated a most extensive hæmorrhagic episode which resulted in death.

Cosgriff *et al.*,[5] Smith *et al.*[6] and others have drawn attention to the problem of thrombosis with ACTH. Bounameaux, van Cauwenberge and Roskam[7] suggested that thrombosis with ACTH is found in those diseases where there is damage to vessels, particularly vascular endothelium, such as lupus erythematosus, periarteritis nodosa, endoarteritis obliterans, Buerger's disease, etc. Here there is present an endothelial lesion tending to thrombosis and it is not surprising that thrombosis then occurs, in view of Cosgriff's finding of increased coagulability with ACTH and cortisone. Stefanini and Rosenthal[8] and others have reported cases of hæmorrhage with ACTH and cortisone. Cheymol and Leroux[9] conclude on the basis of an experimental and clinical study of the effect of ACTH and cortisone on coagulation, platelets, etc., that ACTH will tend to promote hæmorrhage or tend to promote thrombosis, since it causes important modifications of hæmostasis and coagulation, which are markedly different in different patients owing to differences in diathesis. It is evident from our results that treatment with anticoagulants can in itself be one of the factors leading to hæmorrhage with ACTH.

The effect of ACTH in converting rabbits which were previously refractory to dicoumarol to reactors is unexpected. Presumably this is due to the known influence of ACTH on protein metabolism,[10] particularly in the liver. It is interesting that the converted rabbits showed the same mortality with dicoumarol and ACTH as the original group of reactor rabbits.

Why does the combined administration of dicoumarol and ACTH lead to hæmorrhage? It is evident that as the latter does not increase the effect of dicoumarol on the blood prothrombin in reactor rabbits, the ACTH must have some other effect. ACTH causes an increase in the number of platelets[11] but it also decreases their adhesiveness.[7] Roskam, Jaques, MacFarlane, and Tocantins in their respective writings have for many years emphasized that hæmostasis depends on three mechanisms—blood coagulation, platelets, and vascular integrity. Interference with a single mechanism does not result in hæmorrhage. Interference with several mechanisms simultaneously results in hæmorrhage. Dicoumarol interferes with blood coagulation. The similarity of the effects of ACTH to those of stress suggests that, like the latter, ACTH lowers vascular resistance in addition to affecting platelets. The relation of this action of ACTH to corticosteroids is under investigation. However, the observation that hæmorrhagic death did not occur when ACTH was administered daily following dicoumarol is in agreement with other experiments that suggest that ACTH does not have a direct effect but rather that the hæmorrhage is related to levels of circulating corticosteroids below normal, after the initial rise due to administration of ACTH. With damage to two hæmostatic mechanisms, hæmorrhage results. The fact that this occurs in only 20% of animals suggests that not every animal shows the same degree of damage with the dose of ACTH used.

Summary

A significant number of rabbits treated with both dicoumarol and ACTH died of hæmorrhage. No animals died on ACTH treatment alone and only one in 33 died of hæmorrhage with dicoumarol.

Rabbits which failed to show any increase in prothrombin time with a standard dose of dicoumarol showed an increased prothrombin time after treatment with ACTH.

Administration of somatotrophin, cortisone and desoxycorticosterone did not cause death in animals receiving dicoumarol.

A case is reported of gross phlebitis occurring in a patient suffering from rheumatoid arthritis and treated with Tromexan and ACTH. When the two drugs

were given simultaneously, extensive hæmorrhage was observed, particularly from the gastro-intestinal tract. On cessation of the combined therapy, the patient recovered and no other cause of hæmorrhage could be discovered. A second case is reported of extensive, fatal hæmorrhage following treatment with ACTH.

We are greatly indebted to Mrs. L. Horborenko, R.N., and the technical staff of the Department of Physiology for their invaluable assistance in this research.

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RÉSUMÉ

L'administration concomitante de dicoumarol et d'ACTH chez le lapin entraîne la mort d'un certain nombre d'animaux à la suite d'hémorragies viscérales (pulmonaires, rénales et intestinales). L'ACTH par lui-même ne provoque aucune mortalité. Un des 33 lapins traités par le seul dicoumarol a succombé. Dans nos essais les lapins chez lesquels on n'observa aucun accroissement du temps de prothrombine à la suite de l'administration orale d'une dose standard de dicoumarol réagirent normalement à l'anticoagulant lorsqu'ils furent traités à la fois par dicoumarol et ACTH. L'administration de somatotrophine, de cortisone ou de désoxycorticostérone à des lapins traités par dicoumarol n'entraine aucun accroissement de la léthalité.

Les auteurs rapportent deux cas cliniques illustrant leurs observations expérimentales 1) chez une malade souffrant de polyarthrite chronique évolutive compliquée de phlébite, l'administration simultanée de Tromexan et d'ACTH entraîna des hémorragies importantes, particulièrement au niveau du tractus gastrointestinal alors que l'anticoagulant administré seul préalablement à ce traitement combiné avait été parfaitement toléré pendant plus de trois semaines. A l'arrêt de la thérapeutique associée les hémorragies cessèrent, aucune autre cause de saignement ne put être découverte. 2) chez une malade souffrant de lupus érythémateux aigu disséminé avec hypoprothrombinémie des hémorragies généralisées apparurent au cours d'un traitement par ACTH.

SYMPOSIUM ON THE MANAGEMENT OF CORONARY HEART DISEASE*

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[*Each of the authors had undertaken to deliver a 20-minute paper on a broad aspect of coronary heart disease, after a luncheon at the annual meeting of the Canadian Medical Association, Quebec Division. At their first session to consider their tasks, they chose to use a novel technique to present the subject of the management of coronary heart disease. This method is to be found applied to the subject of the rehabilitation of cardiac patients in a recent book edited by Dr. Paul D. White and his confreres.*[1] *Moreover, as both French and English were used by both speakers, a version was prepared in each language; the French version is to be published in* l'Union Médicale.]

1. *How important is coronary heart disease in the daily work of the general practitioner?*

DR. SEGALL: Two elements join to make coronary heart disease of primary importance in the general practitioner's daily work. The total number of men and women in the susceptible age group, i.e., over 50 years, has been and is steadily increasing because of improved public hygiene, life-saving antibiotics and life-saving, life-prolonging surgery. This is one element, the greater number of candidates for the disease. The other is the improved medical knowledge which has made every physician and surgeon acutely aware of the clinical pictures of the disease so that it is recognized more readily in all its varied appearances. The availability of the portable electrocardiograph apparatus has greatly strengthened the physician's diagnostic power. Public education has made lay people fully aware of the wide prevalence of coronary heart disease, its recognition by the physician is not surprising, and lay people tend to give better co-operation in its management because they bring an informed intelligence to bear on the problem.

2. *What guidance does the clinical history provide in recognizing coronary heart disease?*

DR. DAVID: With the exception of rare instances, the diagnosis of coronary heart disease remains based on the *clinical history*. Therefore, the practitioner or the heart specialist must not hurry in taking the history of a disease that will reveal itself by the answers of the patient. What are the clues to be recognized by the examining physician?

First.—It seems to be an established fact that coronary disease is associated with some genetic factors which make it more frequent in certain families and rare in others. Therefore, it is not without interest to know the family history of the parents, brothers and sisters.

Second.—A higher incidence of coronary disease has been observed with certain entities such as hypertension, diabetes, xanthomatosis, familial or essential hypercholesterolæmia, myxœdema, etc.

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Third.—The clinical picture of coronary disease is dominated by one symptom described by Heberden in 1768 as "angina pectoris" which represents a very distinctive "disorder of the breast" associated with "a sense of strangling and anxieties".

Time does not permit discussion of every aspect of the pain which is well known. I would like to limit myself to some criteria in which I strongly believe.

1. Any pain, anywhere in the chest, associated with effort in the broader sense of the word, which includes emotion, anger, and digestion, should suggest the probability of a coronary artery disease syndrome, especially if the pain is rapidly relieved by rest, relaxation or nitroglycerin.

2. Radiation of pain into the left arm is not an essential component of this syndrome.

3. Any pain localized in the retrosternal area and lasting for more than half an hour should be considered as a possible symptom of coronary occlusion.

4. Any "acute indigestion" not associated with frankly abnormal abdominal signs, in a patient over the age of 40, should be seriously investigated to rule out myocardial infarction.

A detailed study of pain should permit the examining physician to assign his coronary patient to one or other of the three following groups:[3]

First Group.—Chronic coronary insufficiency, also described as chronic "angina pectoris". The patient has the classical symptoms on effort and they are relieved by rest or nitroglycerin.

Second Group.—Subacute coronary insufficiency, also described as impending infarction syndrome, prethrombotic insufficiency or premonitory symptoms of infarction. This syndrome must be thought of: (a) when pain in a given anginal patient changes in its character, its intensity, its duration or in its provocation; (b) when any patient experiences his first pain and is seen shortly afterward by his physician; (c) when pain is typical but not well relieved by nitroglycerin.

Third Group.—Acute coronary insufficiency, well known as coronary thrombosis.

It is nowadays important to differentiate these three groups of patients because the therapeutic program will be different for each.

3. *What significant information does the physical examination reveal?*

DR. SEGALL: In many instances, the physical examination reveals not a single clue to coronary heart disease, and the diagnosis depends entirely on the story of symptoms. When positive physical signs do appear they are usually non-specific and must be correlated with the history and laboratory evidence to establish their significance. The experienced physician recognizes the facial expression which suggests not only acute pain but intense anxiety, indeed fear, in a person who is usually well balanced emotionally. And even if the physician does not see the patient during the pain he can often recognize the difference between organic disease and psychogenic symptoms in the patient's manner and expression as he tells the story of his sensations.

In chronic and in subacute coronary insufficiency, no specific physical signs aid in the diagnosis. If any abnormalities should be found, such as hypertension or cardiac enlargement, they tend to support the diagnosis as evidence of the probable presence of coronary arteriosclerosis. A faint first heart sound does not indicate a weak myocardium; it suggests delay in conduction between auricles and ventricles, a non-specific abnormality, from which may be inferred the possible existence of myocardial fibrosis in the region of the bundle of His due to coronary artery disease.

In acute coronary artery disease the physical signs vary from none at all to a great abundance, but in general they are non-specific and must be correlated with clinical history to establish the diagnosis. During the acute severe pain, there may be a greyish pallor, profuse sweating, marked restlessness, coldness of hands and feet, either a slow pulse, as slow as 30 per minute, or more frequently only a slightly accelerated pulse, between 90 and 100, and rarely a very rapid pulse that is uncountable, i.e., more than 180 per minute. The very slow pulse suggests partial or complete heart block. Variations in loudness of the first sound from very faint to very loud as one listens to about 30 consecutive regular beats strongly indicate complete heart block when the rate is slow. If this appears as a new feature during acute coronary insufficiency, then it strongly suggests that the occlusion is situated in the right circumflex coronary artery about 1 cm. from its origin. It is there that the little artery which supplies the region of the bundle of His comes off. Such cases stimulate the imagination of the clinician; he can predict the appearance of the electrocardiogram and the pathological anatomy from his observations with the stethoscope. The very rapid pulse means ectopic auricular or ventricular tachycardia. The electrocardiogram quickly establishes the diagnosis although there are useful clinical guides in the character of the heart sounds which offer strong clues to the correct diagnosis of the arrhythmia. Failure to reduce the rapid rate by carotid sinus pressure, and variations in loudness of first sound, favour the diagnosis of paroxysmal ventricular tachycardia. Only these two abnormalities of rate and rhythm can be mentioned on this occasion. The clinical recognition of cardiac arrhythmias is a separate subject.

The arterial pressure may be normal, high or low. If high, it may be higher than the usual normal pressure in the given individual. This elevation is temporary; it lasts only some hours during and after the acute pain. More often the arterial pressure falls below the usual normal. As long as the sounds heard over the brachial artery

in measuring the pressure remain of about normal loudness, the shock syndrome need not be feared. But as soon as these sounds become faint and indeed almost inaudible, then the shock syndrome most likely exists. During shock the pressure may be as high as 130 mm. Hg systolic and 100 diastolic but usually is lower, about 80 systolic and 60 diastolic.

A pericardial friction rub not only tends to confirm the diagnosis of myocardial infarction but indicates that the lesion involves the anterior aspect of the heart and extends to the epicardial surface. In the presence of a rather large infarct and especially when there is pericarditis, body temperature rises for from several days to about two weeks. It usually rises no higher than 100° F. but may reach 102° and very rarely higher levels.

4. *What does the electrocardiogram add to the clinical picture in chronic and subacute coronary insufficiency?*

DR. DAVID: This question will permit me to underline the fact that a normal ECG is compatible with the diagnosis of chronic or subacute coronary insufficiency. In other words, a normal tracing should never rule out the clinical diagnosis. Too often, I have seen practitioners change their diagnosis for the sole reason that the ECG was normal. It must be remembered that an electrocardiogram is not the equivalent of a consultation. The ECG is essentially an important aid with its limitations like any instrumental technique. Therefore, the interpretation of any ECG must be made in relation to symptoms and signs.

On a statistical basis, it is agreed that about 30% of patients having chronic coronary insufficiency have normal tracings. In this group some may have a clinical picture which may be typical, others may have quite an atypical story. In both, but especially the latter group, it may be very informative to register a tracing after exercise which may, with or without symptoms, elicit some degree of myocardial hypoxæmia in relation to the suspected coronary insufficiency.

Here again, the interpretation of the "after an effort" tracing demands a great deal of caution. Experience has shown the possibilities of false negative and even false positive tracings.

We personally ascribe great significance and high value to the exercise test. But we have learned the importance of quality as well as quantity in this test.

From our group experience of over 1500 exercise tests I would like to summarize our present-day thinking:

(a) The effort test is not dangerous if done on selected patients, with medical supervision, and if the effort is proportioned to the patient's tolerance.

(b) The test is more apt to be positive if it provokes some pain.

(c) The test should be stopped immediately on the appearance of pain.

(d) A true positive test is pathognomonic.

(e) A true negative test does not rule out coronary insufficiency. In this instance, if the clinical history is suggestive, it may be rewarding to repeat a modified test by increasing the speed of the treadmill or placing the 3-steps stair outside or by making the effort immediately after a meal or by having the patient smoke one to three cigarettes before or during the test.

If such effort tests are done with meticulous care, there should be little chance of missing any true case of coronary insufficiency.

In subacute coronary insufficiency the percentage of normal ECG's is much lower than in chronic insufficiency. Usually, some displacement of the S-T segment will confirm the subacute hypoxæmia of the myocardium.

5. *What does the electrocardiogram add to the clinical picture in acute coronary artery disease?*

DR. SEGALL: The answer to this question permits a pleasing brevity. The electrocardiogram not only demonstrates that there is myocardial ischæmia or infarction but very often indicates the part of the ventricle involved and whether the infarct is transmural. However, one must have patience with the puzzling imperfections of the method. For unknown reasons, in some few cases, the electrocardiogram may not show any abnormalities in the first 24 to 48 hours and in some rare cases a week or more may elapse before the expected abnormalities appear. In the meantime the physician must depend on his clinical observations for diagnosis and therapy.

6. *What other laboratory tests aid in confirming diagnosis and assessing severity of the disease?*

DR. DAVID: In atypical chronic or subacute coronary insufficiency the clinical picture may become so confused that it creates a real syndrome, named by Froment the "intricate angina pectoris syndrome". In these cases, all the differential diagnostic possibilities must be eliminated. Radiographs may play a predominant role in confirming or rejecting different conditions such as diaphragmatic hernia, gastric ulcer, cervical disc disorder, or cholelithiasis. We have seen spectacular cures by an appropriate therapy, medical or surgical, in some of these patients whose angina-like symptoms did not represent coronary artery disease. In others, the relief of one curable condition did significantly improve the over-all picture.

In recent years, a few tests have been suggested and applied to widen the limits of our clinical and electrocardiographic knowledge. The most promising are several blood tests which are useful:

(a) In borderline cases in which the differential diagnosis between subacute and acute coronary insufficiency is not always feasible.

(b) In cases where the infarction may be masked on the electrocardiogram by previous alterations such as those of left bundle branch block or of past infarction.

(c) To estimate the extent of the infarction and its fibrous transformation.

The most utilized of these tests is the measurement of *transaminase* (S.G.O.T=serum glutamic oxaloacetic transaminase). The range of this enzymatic product in normal blood varies between 0 and 40 units. The myocardium, which is normally rich in this specific enzyme, liberates it into the blood stream beginning 4 to 6 hours after the coronary occlusion, with a maximum in 18 to 36 hours and a return to a normal range in 4 to 6 days. In myocardial infarction a positive transaminase test is found in 91.5 to 97.6% of cases. But it must be remembered that the test may be positive in 50 to 88% of the following conditions: rheumatic carditis, acute hepatitis, obstructive jaundice, hepatic cirrhosis, pancreatitis, primary or secondary cancer of the liver,[4] hæmolytic anæmia, hæmorrhagic ulcer.[5] On the other hand, the test is negative in borderline conditions such as subacute coronary insufficiency and in pulmonary infarction.[6] The serum lactic dehydrogenase (S.L.D.) is also elevated in myocardial necrosis but this elevation is less marked and more prolonged than the S.G.O.T.[7]

The fibrinogen plasma concentration, the serum aldolase and C reactive proteins (C.R.P.A.) have also been studied and are positive in myocardial necrosis. The fibrinogen test is a good index for the estimation of the recovery process. It should become normal in the second or third week after the infarction.[8]

I will only mention the importance of the white blood cell count and sedimentation rate, whose variations are well known to all of you.

7. *What are the principal elements of the therapeutic program for chronic and subacute coronary insufficiency?*

DR. SEGALL: The patient who has cardiac pain of chronic coronary insufficiency, so-called angina pectoris, and reports at his first visit that many weeks or months have elapsed since he first felt the pain, should be advised to continue with his usual way of life with some reservations. He should be advised to avoid those conditions which act as trigger mechanisms to bring on the pain. The more common of these are (1) a sense of hurry even while seated in a car, in a train or a plane; (2) hurry in walking; (3) walking outdoors immediately after a meal, even a small meal; (4) walking against a wind or in cold weather; (5) walking up an incline; (6) excitement developed in quarrels or in watching a wrestling match but not a boxing match, probably because he identifies himself with a wrestler and not with a boxer. I have known patients who avoid having the pain in viewing a hockey game on television, by turning off the sound so as to eliminate the excitement transmitted by the commentator.

The patient should be instructed in the use of tablets of nitroglycerin, grain 1/100, for the prevention and relief of the cardiac pain. He should be given a pill, placed under the tongue, to test whether it causes pounding in the head or reduction in blood pressure to levels which induce a sense of faintness. In the great majority of people neither of these symptoms occurs. The patient may be assured that nitroglycerin, even 20 or more tablets per day, taken singly at intervals of about 15 minutes, can cause no harm. Moreover, he should be told that it is not a narcotic and not habit-forming and therefore he may use it liberally. A pill placed under the tongue before a necessary walk outdoors may prevent the pain, and if it should appear another pill should be taken to relieve it. The earlier the pill is taken, the shorter the duration of the pain. Recently a tablet containing grain 1/25 has become available: its effect may last about an hour. Nitroglycerin has been found to be effective in preventing cardiac pain which tends to occur during coitus, which need not be prohibited.

It is rare for us to meet with cases in which the person's work involves exertion or excitement which brings on the pain; in such instances a change of occupation becomes necessary. Many patients report that they cannot understand why exertion indoors and much walking indoors can be performed without pain but walking for three minutes from home to the bus results in pain. There is, indeed, something specific about walking outdoors as a trigger mechanism for initiating cardiac pain of chronic coronary insufficiency.

In 1945, after analyzing 1400 cases of coronary heart disease which I had observed between 1926 and 1944, I learned that patients with subacute coronary insufficiency symptoms develop the acute form usually within two weeks after the onset of the subacute; hence the designation—prodromal syndrome of coronary occlusion. Therefore, once the subacute type is recognized the patient is ordered to remain at home or in hospital on a convalescent regimen until 14 consecutive days have elapsed without any cardiac pain. The patient who begins to have chronic coronary insufficiency symptoms only a day or so before his visit to the physician, requires treatment of the same kind as a subacute type, because his symptoms may be the earliest warnings of acute coronary occlusion. Before the advent of anticoagulants about 20% of subacute cases developed coronary artery occlusion; I have not yet analyzed my own experience, but some authors have reported a reduction in this frequency and it does seem logical that such patients should be given anticoagulants, not only during the two or more weeks of preventive treatment but subsequently for an indefinite length of time. Those patients who accept the

risks and choose to co-operate should be given chronic anticoagulant therapy.

In addition to nitroglycerin, these patients should have a strong sedative to take for pain which is not relieved by nitroglycerin. I usually prescribe 50 mg. tablets of meperidine (Demerol), one to be taken every 15 minutes for four doses during persistent pain. To this, the instruction is added that after taking the first meperidine tablet the patient should call for the physician. This provides him with effective sedation while waiting for the doctor to come in order to assess the significance of the pain. Usually a diagnosis of either subacute or acute coronary insufficiency is made, the former a threat of myocardial infarction and the latter the signal of existing infarction.

The so-called vasodilators—Aminophyllin, Peritrate, Metamine, or any others—may be prescribed. Their pharmacological effects leave much to be desired, but for a few weeks or months they may have a good psychological effect on both physician and patient.

8. *What are the principal elements of the therapeutic program for acute coronary insufficiency with myocardial infarction?*

DR. DAVID: The mortality in acute coronary insufficiency is especially high in the first 48 hours.[9] Therefore, the attending physician must try, as quickly as possible, to classify his patient as a bad-risk or a good-risk case.

Within the limits of these first 48 hours, I would consider as a bad-risk patient anyone showing one or more of the following factors:

(a) Persistence of pain despite adequate sedative medication.

(b) Presence of symptoms and signs of shock.

(c) Presence of acute or subacute heart failure.

(d) Presence of any marked modifications of the heart rate or rhythm.

The bad-risk patients should be urgently hospitalized with the main objective of using all known therapy to relieve pain, shock, and heart failure or to restore a normal rate or rhythm.

Especially with patients in shock or in acute heart failure, time has a vital importance. I have seen very few survivors when this complication was not adequately treated in the first six hours. Of course, it must be remembered that, even with well-conducted treatment, mortality remains high in this situation, but considerably lower than ten years ago.

The other group of patients, the so-called good-risk patients, can be treated in their homes.

I would like to concentrate the discussion on only two aspects of the treatment because some different points of view have been expressed and more experience is needed before one may become dogmatic. These two points are: anticoagulant therapy and bed rest.

1. *Anticoagulant therapy:*

For statistical purposes we have determined the length of illness in acute coronary insufficiency as being eight weeks. The problem is to state whether anticoagulant therapy will significantly benefit the patient during these eight weeks. This benefit is judged by studies of comparative mortality and incidence of complications in patients receiving and those not receiving anticoagulant therapy.

I. Wright and H. Russek are the best representatives of two opposite ways of thinking. Wright[10] maintains that with anticoagulant therapy, in any series of more than 250 cases, the immediate mortality is decreased in a percentage varying from 50 to 33%. Russek[11] thinks that anticoagulant therapy is useless in the so-called "good-risk" patients; he found a mortality rate of only 3.3% in such cases without anticoagulants.

Because of this divergence of opinion it would seem reasonable to give anticoagulants mainly to the bad-risk patients for whom we have already suggested hospitalization. On the other hand, we wish to emphasize the important place of anticoagulant therapy in the prophylaxis of coronary insufficiency. Therefore, for this purpose, we give routinely an anticoagulant drug to all patients who will lend themselves to such treatment indefinitely. In a follow-up series, our associate, Dr. Y. Desrochers, has proved the harmlessness of short-term and long-term anticoagulant therapy when the doctor has gained experience with a particular substance, when the patient is co-operative, and when adequate laboratory facilities are available.

2. *Bed rest versus armchair treatment:*

Since 1937, our co-panelist, Dr. Harold Segall, has permitted bathroom privileges, movements in bed, and sitting in a chair in apparently good-risk patients beginning after the third or fourth day of illness. Samuel Levine in 1952[2] strongly advocated early rehabilitation with armchair treatment.

We have personally adopted an intermediate position which is dictated mostly by the severity of the attack. In every case we prescribe a minimum of two weeks' bed rest. Depending on the clinical evolution, the extension of the infarction, the psychological attitude of the patient, we then rehabilitate the patient slowly or rapidly. As an average, we consider that the patient should be partly or completely back to work three to four months after the beginning of the illness.

9. *How would you state the prognosis and how would you guide rehabilitation?*

DR. SEGALL: I think that whether we physicians are aware of it or not we practise the art of rehabilitation based on our concept of prognosis as soon as we begin to speak to a patient of his

illness and its treatment. The whole subject can be dealt with briefly, as when the doctor says, "Your heart is affected, but not very badly; just take it easy." This leaves it to the patient to use his own judgment in arranging his affairs and setting the limits of his activities. Brevity is admirable but the great majority of patients desire and deserve more detailed treatment of this subject.

How long the patient will live; when he will have a fresh attack of acute coronary insufficiency with myocardial infarction; whether such illness will be followed by congestive cardiac failure, cannot be predicted in any given case. The statistical information derived from the analysis of large series of cases helps to guide the physician, as does the knowledge about individual patients who have lived 25 or more years after the onset of coronary heart disease. The wide gap of ignorance must be filled with so-called commonsense judgment. An optimistic prognosis is more often right than wrong, and produces better therapeutic results than a pessimistic mood created by what the doctor says or implies.

The patient with chronic coronary insufficiency should be advised to continue his usual type of work if it does not act as a trigger mechanism to produce pain. The patient with acute coronary insufficiency and myocardial infarction who feels "condemned" to remain at rest for six to eight weeks can be cheered up most effectively if he is told that at the end of the illness, after convalescence of about two weeks, he will be able to return to his usual form of work. In the majority of cases this does occur. A few—those who develop congestive cardiac failure—must curtail activities; but adjustments can be made so that they find gainful employment in suitable jobs. From my own experience as well as what appears in the literature on rehabilitation of people with coronary heart disease, motivation plays the dominant role in the success or failure of good adjustment. Those who become totally disabled are less often suffering from cardiac pain or congestive cardiac insufficiency than from psychological disability initiated by the acute illness or by simply becoming aware of the existence of heart disease. In most of these cases the patient has had some difficulty in adjusting himself to life in the past because of a personality defect. It is difficult to find precisely the proper phrases for each patient but the doctor must try to speak to each individual according to his own merits, addressing himself to a human being and not alone to the diagnostic label which he places on the patient. The physician's objective must be to guide the patient in remaining as useful as possible to himself, to his family and to society in general. The best measure of the person's capacity to work and play is found in noting his performance at work and at play. There is no other reliable means of measuring the human being's physical and mental reserves of strength than the test of actual performance.

10. *What are the ways and means of preventing coronary disease?*

DR. DAVID: Atherosclerosis of the coronary arteries is responsible for nearly all cases of coronary insufficiency. Therefore, the over-all problem of prevention depends on prophylaxis of atherosclerosis. This is one of the greatest challenges of modern medicine. Success in its prevention would prolong significantly the average length of life and would prevent catastrophes too often associated with sudden death or prolonged invalidism. A nation-wide research program guided by renowned authorities would seem the only logical way to deal with such an important and urgent problem. It may happen that the human being has not been able to adjust his arteries to the world he has created, but it still has to be proved. I feel that the problem of atherosclerosis can be solved if humanity is willing to devote as much energy, intelligence and financial resources to a co-ordinated research program as it has effectively devoted to creation of modern destructive weapons. Prevention of atherosclerosis is a problem which concerns everybody if one bears in mind that, after the age of 40, one human being out of two will suffer from it.

A sound knowledge of the many different factors involved in atherosclerosis is important since its prophylaxis will aim to affect these factors. Which are the principal?

1. *Age:*

Until recent years age and atherosclerosis were closely related in everybody's mind. We cannot deny a certain relation between age and hardening of the arteries, but it is more and more evident that the aging theory represents mainly an easy escape from facing the facts. Atherosclerosis must be considered a preventable disease rather than an inevitable result of aging.

2. *Heredity:*

Every experienced practitioner and cardiologist has been impressed by the high incidence of atherosclerotic heart diseases in some families. The strange coincidence of some reported cases of coronary insufficiency happening at the same age in some "twins" is striking.[12, 13]

3. *Mechanical factors:*

It seems that atherosclerosis is more apt to develop in the arteries which face the thrust of the blood ejected in their lumina by the systole of the heart.

It has also been shown that the atherosclerotic lesions are more apt to be seen at bifurcations, at points of flexion and in less well supported arteries.[14]

4. *Stress:*

Many laymen and physicians have tried to correlate a seemingly higher incidence of coronary diseases nowadays with the superdynamic modern life. In recent animal experiments, Hans Selye[15, 16] has shown that in certain conditions he could produce myocardial infarctoid necrosis which may be prevented by the administration of some substances. This new experimental pathway may be a very important one but at present, no absolute relationship between coronary disease and stress has been established for man.

5. *Hormonal factors:*

All statistics show a lower incidence of coronary disease in women than in men until the age of 50 to 60. The proportion varies from 6 to 1 to 2 to 1. These differences demonstrate that the female is protected by her sexual hormones.[17] Clinical experience with women having early coronary insufficiency often reveals early castration in the past medical history. The pathways of the hormonal protective mechanisms are still unknown.

6. *Fat metabolism:*

Many correlations have been found between the incidence of coronary disease and the metabolism of fats, mainly cholesterol.[18] They have justified the current tremendous research on fat metabolism. Progress is rapid and sometimes confusing. Let us try to summarize what appear to be the most important proven data.

(a) Man eats two main types of fats: animal and vegetable. As a rule, ingestion of vegetable fats does not tend to increase cholesterol, as compared with animal fats.[19, 20]

(b) This difference in these two types of fats is mainly due to their content of saturated and unsaturated fatty acids. Unsaturated fats are less atherogenic than the saturated.

(c) Even in the unsaturated fats, there are differences depending on the molecular structure of the fatty acids. The differences lie in the number of carbon atoms not bound with hydrogen. The more such carbon atoms there are, the less is the fatty acid saturated.

(d) The fats utilized by man usually are a mixture of saturated and unsaturated fatty acids. The total unsaturation of a fat can be studied by its iodine index, which represents the number of hydrogen atoms available for replacement by iodine.

7. *Coagulation factors:*

Coronary thrombosis is essentially related to the coagulation mechanism of blood in an atherosclerotic artery. For this reason, as already stated, anticoagulant therapy has been advocated and numerous reports have shown its beneficial long-term results.[21, 22]

In conclusion, we feel that prophylaxis will have to deal with all these factors and not adhere to a single theory. At present we cannot expect a full guarantee of security even for the patients who will follow our advice rigidly and co-operatively, because some factors of atherosclerosis cannot be changed, such as heredity and sex. On the other hand, it is logical to utilize what is known and feasible, such as a balanced way of living, dietary regulation and anticoagulant therapy.

SUMMARY

Coronary heart disease is probably more common now than typhoid fever used to be 50 years ago. Physicians must be fully informed about this disease so that they may recognize its various types. Its classification into three degrees of intensity of illness conveniently guides in its management. Chronic coronary insufficiency, so-called angina pectoris, is the mildest degree: subacute coronary insufficiency, also known as the prodromal syndrome of coronary thrombosis or by the confusing name acute coronary insufficiency, causes the physician most anxiety; about one in five such persons develop acute coronary occlusion with myocardial infarction, i.e. what we here call acute coronary insufficiency, within about two weeks after the onset of the subacute phase. In many cases of acute coronary insufficiency with myocardial infarction, no warning symptoms occur.

Each patient requires individual treatment. He must be educated to live with the disease very much as a diabetic must be educated in order to achieve the best in treatment and the most in rehabilitation.

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RÉSUMÉ

Les pages qui précèdent reproduisent le texte d'un colloque sur le traitement des maladies des coronaires, tenu à l'occasion de la récente réunion annuelle de la Division du Québec de l'Association médicale canadienne. Le docteur Harold N. Segall et le docteur Paul David sont d'avis que la maladie des coronaires est probablement plus fréquente de nos jours que ne l'était la typhoïde il y a 50 ans. Les médecins doivent être bien renseignés au sujet de cette affection afin de pouvoir en dépister toutes les variantes. Son classement en trois degrés d'intensité facilite la con-

duite du traitement. L'insuffisance coronarienne chronique également connue sous le nom d'angine de poitrine en représente la forme la moins intense; l'insuffisance coronarienne subaiguë ou syndrome prodromique de la thrombose coronarienne est également connue sous l'appellation (qui porte à confusion) d' "insuffisance coronarienne aiguë". Elle est sans doute la forme qui cause le plus d'inquiétude aux médecins car environ un cas sur cinq est atteint d'occlusion aiguë coronarienne avec infarctus du myocarde environ deux semaines après le début de la phase subaiguë. Dans plusieurs cas d'insuffisance coronarienne aiguë avec infarctus du myocarde on ne trouve aucun symptôme prémonitoire. Le traitement demande à être adapté individuellement à chaque malade. Le patient doit apprendre à vivre avec son affection tout comme le diabétique doit le faire, afin d'atteindre les meilleurs résultats non seulement au point de vue du traitement mais aussi au point de vue de la réadaptation.

MESENTERIC INFARCTION*
A CLINICAL STUDY OF 49 CASES

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GREAT ADVANCES have been made in the treatment of intestinal obstruction and thrombo-embolic disease in the past two decades, but in mesenteric infarction, which presents features of both of these conditions, there has as yet been no appreciable reduction in mortality. This investigation was carried out in an attempt to provide some reasons for the continuing high mortality from mesenteric infarction.

It is based on a clinical study of all cases treated at the Vancouver General Hospital during the ten-year period 1947-1956. Only those cases in which the etiological agent was clearly established at laparotomy or at autopsy were included. A number of cases designated as venous infarction were excluded because the thrombosis was quite localized, and obviously secondary to such mechanical effects as volvulus, or strangulation by adhesive bands. There were also a few cases of massive mesenteric thrombosis associated with extensive systemic venous and arterial thrombosis which could only be regarded as a terminal event in a moribund patient. These too were excluded. Forty-nine well-documented cases were left. This group represented 0.016% of the total hospital admissions during that time – an incidence of approximately one in 6000 admissions.

INCIDENCE OF CORRECT CLINICAL DIAGNOSIS

It should be emphasized at once that one of the main problems was that of diagnosis.

For the entire series the correct clinical diagnosis was made in 17 or 35% (Table I). Twenty-seven patients were admitted because of the disease. In this group the correct diagnosis was made on admission or shortly thereafter in 11 or 41% of cases. Twenty-two or approximately 44% of patients developed mesenteric infarction during the course of hospitalization, usually for arteriosclerotic heart disease. Under these circumstances, the correct diagnosis was made in only six cases or 27%. With ample opportunity for close observation of the patient, it is difficult to account for this discrepancy. I suspect that in most cases the gravity of the primary illness distracted the clinician from serious consideration of the abdominal complaints. The rate of diagnosis under all circumstances was somewhat better than that generally reported.

TABLE I.—INCIDENCE OF CORRECT DIAGNOSIS

		Correct clinical diagnosis
All cases	49	17 - 35.0%
Admitted with infarction	27	11 - 40.7%
Infarction developed during hospitalization	22	6 - 27.3%

*Read at the Annual Clinical Meeting of the B.C. Surgical Society, Harrison Hot Springs, May 1-3, 1958.

ETIOLOGY

In this series there were 29 women and 20 men. The youngest patient was 27 years of age; the oldest, 89 (Table II).

TABLE II.—AGE DISTRIBUTION BY DECADES

21 - 30	1	61 - 70	21
31 - 40	0	71 - 80	15
41 - 50	4	81 - 90	5
51 - 60	3		

TABLE III.—ASSOCIATED CARDIOVASCULAR DISEASE (79.6%)

Arteriosclerotic heart disease	28
Rheumatic heart disease	6
"Ulcerative" arteriosclerosis of aorta	3
Acute bacterial endocarditis	1
Cleido-cranial dysostosis	1

Cardiovascular disease was an important etiological agent, being present in 39 patients (79.6%).

Abdominal aortic aneurysm was not present in any case.

The vascular occlusion was arterial in 37 (approximately 75%) and venous in 10 (about 20%). In two there was both arterial and venous occlusion.

Arterial embolism was present in 40% of the series. The embolus was in the superior mesenteric artery in 17 cases, the ileo-colic in 2 cases, and the superior and inferior mesenteric arteries in one case. Both cases of ileo-colic embolism went on to secondary thrombosis of the main trunk of the superior mesenteric artery.

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The embolus arose from the left atrium (fibrillation) in eight cases, a left ventricular mural thrombus in seven cases, a thrombosis over an atheromatous plaque in one case, a septic endocardial vegetation in one and an unknown source in three cases.

Arterial thrombosis was sometimes associated with atheromatous involvement of the superior mesenteric artery (Table IV). The extent of

TABLE IV.—ARTERIAL THROMBOSIS (34%)

Superior mesenteric artery only		11 cases
Superior mesenteric artery, large branch		1 case
Inferior mesenteric artery alone		1 "
Combined	Cœliac and S.M.A.	2 cases
	Cœliac, S.M.A. and I.M.A.	1 case
	S.M.A. and I.M.A.	1 "

narrowing of the superior mesenteric artery was not recorded in all cases. Where the observation was made, the lesion was found to vary from a narrowing of only the aortic orifice of the superior mesenteric artery, to 7 cm. of its length. In most cases only 3 cm. or less was involved.

Venous thrombosis was present in 20%; the superior mesenteric vein was thrombosed in six cases, peripheral mesenteric veins in three, and the inferior mesenteric vein in two cases.

In two patients there was combined peripheral mesenteric arterial and venous thrombosis which produced infarction of the distal ileum. Both patients recovered after resection.

Previous Embolic Phenomena

Three patients suffered systemic arterial embolization preceding mesenteric infarction. One patient had a popliteal embolism two years before the final superior mesenteric embolism. One male patient was admitted to hospital with axillary embolism which was treated medically. Thirty-six days later, superior mesenteric embolism occurred for which an embolectomy was performed. A third patient had a leg amputation because of popliteal embolism. He died of mesenteric venous thrombosis one week after operation.

"Delayed" Mesenteric Infarction

Twelve patients, approximately 25%, displayed vague prodromal symptoms lasting for several days to a week or more before the onset of infarction. It was found that they more often suffered a mesenteric thrombosis, arterial or venous, than an embolism, but this finding was not constant.

The prodromal symptoms were by no means diagnostic and consisted mainly of mild abdominal cramps, occasional nausea or vomiting, and diarrhœa more rarely. Symptoms usually appeared after meals.

In one patient these symptoms lasted for a month, and on several occasions occult blood was found in the stools. He finally succumbed to superior mesenteric venous thrombosis. A 61-year-old woman suffered from crampy upper abdominal pain after meals for seven months. She was considered to have an abdominal aortic aneurysm with "abdominal angina" secondary to superior mesenteric artery insufficiency. She died from superior mesenteric artery thrombosis with infarction of the small bowel several days after attempted aortography. At autopsy an aneurysm was not found, but there was extreme arteriosclerotic narrowing of the aortic orifice of the superior mesenteric artery, with distal thrombosis.

Symptomatology

It is generally reported that the severity of symptoms of mesenteric infarction is greater when the vascular occlusion is caused by embolism rather than by arterial or venous thrombosis. In this study it was evident that the severity of symptoms depended more on the size of the occluded vessel and the consequent extent of infarction than on the type of occlusion.

The most constant symptom was abdominal pain, but it was in no way characteristic of the underlying disease. Initially it was of a severe cramping nature; it was mid-abdominal or generalized, and sometimes radiated to the back. After a period of hours, the pain became more constant and was associated with abdominal distension. In those cases where auscultation was carried out, it was noted that bowel sounds were absent, but this was some hours after the onset of the attack. It should be stressed that in a few patients, despite extensive infarction, abdominal pain was almost negligible, and even shock was not pronounced until shortly before death.

Vomiting was present in 33 cases and was variable—from occasional to incessant. One patient with superior mesenteric venous thrombosis had massive hæmatemesis.

Shock as evidenced by such signs as sweating, pallor, rapid pulse and falling blood pressure was a notable feature in less than one-third of cases. When it was present, there was always an extensive mesenteric infarction. As mentioned before, shock was not always an accompaniment of extensive infarction.

Melæna

In the classical description of this disease much importance is attached to the occurrence of melæna, and it is of great value in establishing the correct diagnosis. Unfortunately, it was present in only 10 patients. Of these, the diagnosis was made clinically in six. Diarrhœa without melæna was present in three patients.

Physical Signs

The physical findings were those of acute intestinal obstruction and in no way specific. Tender-

ness was generalized and not severe. The abdominal wall was tense rather than rigid, and usually tympanitic. Bowel sounds disappeared in a few hours after the onset of severe pain in the case of massive infarction, but persisted longer in others.

White Blood Cell Count

The white blood cell count was generally 20,000 or over with a high proportion of polymorphonuclear cells. In a small proportion there was no leukocytosis.

Radiological Findings

X-ray examination, in the form of scout films of the abdomen, was done in 21 patients. The findings were reported as negative in seven. In one patient, radiography was repeated several times over a two-day period, and despite negative findings, autopsy a short time later disclosed superior mesenteric embolism with infarction of the entire small bowel and the proximal one-half of the colon.

Radiologists have reported two findings on scout films to support the diagnosis of mesenteric infarction: (1) the presence of continuous loops of gas-filled dilated bowel corresponding to the infarcted area – particularly terminal ileum and ascending colon in continuity; (2) separation of adjacent loops by the thick congested bowel wall. Neither of these signs was present. Generally the report was of ileus or scattered gas in small bowel or colon, suggestive of mechanical obstruction. It is hard to account for the negative findings. Reich and Love[1] attribute it to the gas in the bowel being displaced by extensive intraluminal hæmorrhage.

Other Tests

In several cases amylase determinations were made because acute pancreatitis was suspected. The levels were within normal limits. No other diagnostic tests were performed.

Jensen and Smith from the University of Minnesota[2] discussed the value of diagnostic peritoneal aspiration. In 78% of their cases the ascitic fluid was bloody. This would be a most valuable test if positive. In this study, it was noted that at autopsy the presence of bloody peritoneal fluid was a universal finding.

MESENTERIC INFARCTION ARISING IN HOSPITALIZED PATIENTS

Five cases developing during the postoperative period merit special attention (Table V).

The correct clinical diagnosis was made in the first two cases listed. In the first, resuscitation failed and surgery was withheld. In the second, 4-5 feet (120-150 cm.) of terminal ileum were resected, and postoperatively anticoagulants were given. The patient survived three months, only to die of septic complications.

TABLE V.—POSTOPERATIVE MESENTERIC INFARCTION

Surgical procedure	*Time of onset after operation*	*Occlusion and extent of infarction*
Resection sigmoid	4 days	Peripheral veins; entire small bowel
Abdomino-perineal resection	6 days	Peripheral arteries and veins; distal ileum
Laparotomy: carcinoma of pancreas (splenectomy)	12 days	Thrombosis sup. mesent. vein; entire small bowel
Closure ileal fistula	6 days	Thrombosis peripheral arteries; distal ileum
Resection small bowel	1 day	Thrombosis sup. mesent. vein; entire jejunum

Seventeen cases developed during the course of hospitalization for medical conditions (Table VI).

TABLE VI.—CONDITION COMPLICATED BY MESENTERIC INFARCTION IN HOSPITALIZED MEDICAL CASES

Arteriosclerotic heart disease	11
Rheumatic heart disease	1
Arteriosclerotic occlusion left common iliac	1
Acute bacterial endocarditis	1
Pneumonia	1
Suspected aortic aneurysm	1
Axillary embolism	1

Only three patients had prothrombin times within the therapeutic range at the time of infarction. In the last noted, embolectomy was performed but was followed by progressive distal thrombosis and infarction of the entire small bowel.

OPERATION

Operation was performed on 14 patients from 12 hours to 4 days after the onset of acute symptoms. Of the two patients recovering, one was operated on 3 days and the other 12 hours after the onset.

In six patients the operation consisted of exploratory laparotomy only. In five, nothing further was done because of the extent of infarction (usually the entire small bowel and right colon). The presence of early mesenteric infarction was not recognized at laparotomy in a 45-year-old obese female patient. She died on the second postoperative day. Autopsy disclosed the presence of infarction of the entire small bowel secondary to atheromatous narrowing and thrombosis of the first inch of the superior mesenteric artery. In this regard, Shaw and Rutledge[3] point out that at laparotomy more information can be gained by palpating the main superior mesenteric artery for pulsations than from the appearance of the bowel. In the early stages of mesenteric arterial occlusion, the intestine may appear almost normal as to colour and peristalsis.

No massive resections were performed. Six patients had limited resections. In two patients this was a right hemicolectomy for infarction of the colon secondary to ileo-colic artery embolism. One patient died one hour after operation, and the other after several days from extension of thrombosis to the superior mesenteric artery. Two patients had venous infarction of the jejunum; 10 feet and 3 feet were resected respectively. The thrombosis extended and the patients died. Two patients had resections of the terminal ileum 6 feet and 10 feet in length, infarcted by combined arterial and venous thrombosis. Both survived for considerable periods. Of the patients undergoing resection, only one who survived received anticoagulants postoperatively.

A 63-year-old male had a superior mesenteric embolectomy. This patient had been admitted 36 days previously with congestive heart failure and axillary embolism which was treated medically. Twelve hours after mesenteric embolism, a laparotomy was performed. Almost the entire small bowel was cyanosed. The superior mesenteric artery was exposed both above and below the transverse mesocolon. Fragments of emboli 2 cm. and 7 cm. long were removed and a good flow of blood was secured from both the proximal and distal ends. Postoperatively, progressive thrombosis ensued despite heparinization, and the patient died of infarction of the entire small bowel.

Resection and Extent of Infarction

There are now many cases of massive bowel resection on record which indicate that 80% or more of the small intestine can be sacrificed without producing serious nutritional disturbances in the patient. In this series the exact extent of infarction was noted in all cases at autopsy. In ten patients there was sufficient non-infarcted bowel present to have permitted survival had operation been performed – other conditions being favourable.

Anticoagulants

It was astonishing to find how infrequently anticoagulant therapy was utilized. Only two patients upon whom operation was performed received anticoagulants. These cases were previously described.

Nelson and Kremen,[4] performing experimental superior mesenteric arterial and venous ligations on dogs, demonstrated the value of heparinization. When the vein was occluded for four hours death occurred in all dogs, but heparinized animals did not die even if the vein was clamped for as long as six hours. Even after permanent ligation, only two out of eight dogs died. The results were not as good for arterial occlusion, but even here great benefit was obtained with heparinization. When the artery was occluded for four hours, 75% of the heparinized dogs survived, as compared with only 25% of the controls.

It is recognized that a more adequate collateral circulation is present in both the mesenteric arteries and veins of the dog, so that it would be dangerous to apply these principles directly to the human subject. However, reports in the literature of survival after mesenteric vascular occlusion treated by anticoagulants alone indicate that they are probably of considerable value.

SUMMARY

The case histories of 49 patients suffering from mesenteric infarction were studied.

The correct clinical diagnosis was made in 35%.

Almost 80% of patients suffered from concomitant cardiovascular disease.

The vascular occlusion was arterial in 75%, venous in 20%, mixed in 5%. Arterial embolism accounted for 40% of cases, while arterial thrombosis was the second most frequent type of occlusion with 34%.

Twenty-five per cent of patients had vague prodromal symptoms of several days' to several weeks' duration preceding the onset of infarction.

An analysis of the presenting symptoms showed that these did not always conform to the dramatic qualities depicted in the classical description of the disease. Shock was a notable feature in less than one-third of cases, while in a few patients symptoms and signs were almost negligible, despite extensive infarction. Melæna occurred in 20%.

Findings on scout x-ray films failed to conform to any diagnostic pattern.

Diagnostic peritoneal aspiration is discussed.

A substantial proportion of cases developed during hospitalization for other diseases, usually cardiovascular —only 27% were correctly diagnosed clinically.

The various operative procedures carried out in 14 patients are described. Only two patients, who had limited resections, survived. At laparotomy early arterial mesenteric infarction may be difficult to recognize from inspection of the bowel alone.

The merits of the use of anticoagulants are discussed.

CONCLUSIONS

The greatest contributing factor to the continuing high mortality from mesenteric infarction is the failure to make an early clinical diagnosis. Abdominal pain developing in the elderly patient suffering from cardiovascular disease, particularly if he is hospitalized, should make the clinician wary of the possibility of mesenteric infarction. Early peritoneal aspiration is probably of considerable positive diagnostic value.

If any criticism of the surgical management in this series is justifiable, it might be that of the failure to make full use of anticoagulants in the postoperative period.

It is to be hoped that as earlier recognition of the condition becomes more general it will become possible to use the established techniques of peripheral vascular surgery. Thus, when the main stem of the superior mesenteric artery has been occluded by an embolus, embolectomy would be the procedure of choice. For those patients displaying prodromal symptoms, in whom arteriosclerotic narrowing of the superior mesenteric artery can be demonstrated radiologically, elective arterial surgery may be feasible.[5]

But for the present, in the great majority of patients exploratory laparotomy will continue to reveal the

presence of infarcted and frankly gangrenous bowel. For them, generous resection and the use of anticoagulants in the postoperative period offers the greatest chance for recovery from this lethal disease.[6, 7]

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RÉSUMÉ

L'auteur rapporte les faits cliniques de 49 malades atteints d'infarctus du mésentère. Le diagnostic clinique fut correctement posé dans 35% des cas; environ 80% des malades souffraient d'affections cardio-vasculaires. L'occlusion vasculaire portait sur les artères dans 75% des cas, sur les veines dans 20% et sur les deux systèmes dans 5%. L'embolie artérielle fut incriminée dans 40% des cas alors que la thrombose artérielle se classait en second avec une fréquence de 34%. Un quart de ces malades accusèrent de vagues symptômes pendant plusieurs jours voire même plusieurs semaines avant l'accident vasculaire. L'analyse de ces symptômes montre qu'ils ne se conformaient pas toujours à la description classique du tableau clinique que l'on est censé voir dans cette maladie. Moins d'un tiers des patients étaient en état de choc alors que quelques malades montraient des symptômes quasi-négligeables en dépit de lésions étendues. On n'observa de melæna que dans 20% des cas. La radiologie ne fut pas d'un grand secours. L'auteur s'étend sur les différentes techniques opératoires employées chez 14 malades. On ne compte que deux survivants chez qui l'on pratiqua une résection de peu d'envergure. Il n'est pas toujours facile à la laparotomie de reconnaître par la seule inspection de l'intestin la présence d'un infarctus mésenterique artériel précoce. L'auteur donne ses vues sur l'emploi des anticoagulants.

THE SURGICAL TREATMENT OF TRANSPOSITION OF THE GREAT VESSELS
REPORT OF TWO CLINICAL CASES*

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TRANSPOSITION of the great vessels is a relatively common form of congenital heart disease. Keith[1] estimates that the lesion occurs once in every 11,000 of the child population. Only ventricular septal defect (1:4000), patent ductus arteriosus (1:5500) and tetralogy of Fallot (1:8500) are more frequently encountered than transposition. Transposition of the great vessels, however, is the most common congenital heart lesion causing cyanosis in the neonatal period.

DIAGNOSIS

The diagnosis of transposition of the great vessels is not usually difficult. However, if the child is to survive even for a short time, cardiac shunts must be present, which permit mixing of blood between pulmonary and systemic circulations. The accurate diagnosis of these associated lesions is frequently difficult and often is impossible until postmortem examination.

The vast majority of infants with transposition are cyanotic, and their cyanosis is usually severe. Dyspnœa is common. In one-third of cases no murmur is heard, but in others a systolic murmur of variable intensity is present. The pulmonary second sound is usually quite loud and is split. The heart is usually slightly to moderately enlarged during the first week of life, and gradually increases in size over the next few weeks or months. Radiologically the heart has a characteristic outline with an extremely narrowed waist. The thymic shadow is usually markedly diminished or absent. The pulmonary vascular markings are increased, unless there is associated pulmonary stenosis. Most cases show electrocardiographic evidence of right ventricular hypertrophy or combined ventricular hypertrophy. The diagnosis is usually easily confirmed by angiocardiography.

PROGNOSIS

The prognosis in transposition of the great vessels is extremely poor. Keith[1] states that the average duration of life is three months, 37% dying in the first month of life and 72% dying in the first six months of life. Although they are relatively rare, exceptions do occur, and in Kato's[2] review he included a patient with transposition of the great vessels who survived to the age of 56 years.

SURGICAL TREATMENT

A tremendous effort by numerous investigators[3-8] has been expended in the attempt to find a successful operation for the treatment of transposition of the great vessels. In 1956, Baffes[9] first described his procedure and presented the successful application of his technique in one clinical case. The operation consisted essentially of transposing the inferior vena cava from the right atrium to the left atrium, and transposing the right pulmonary veins from the left atrium to the right atrium. This partially transposes the venous flow to the heart, and allows for a better exchange of blood between the pul-

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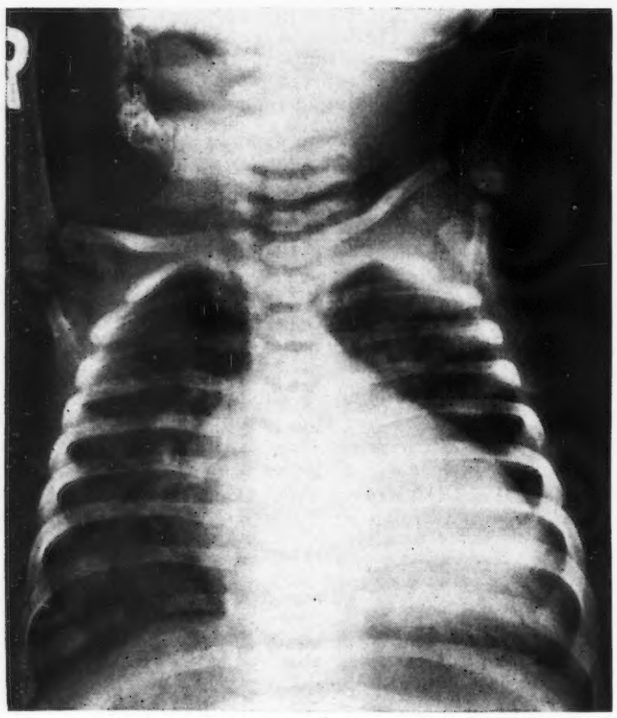

Fig. 1.—X-ray appearance of the heart in typical case of transposition of the great vessels.

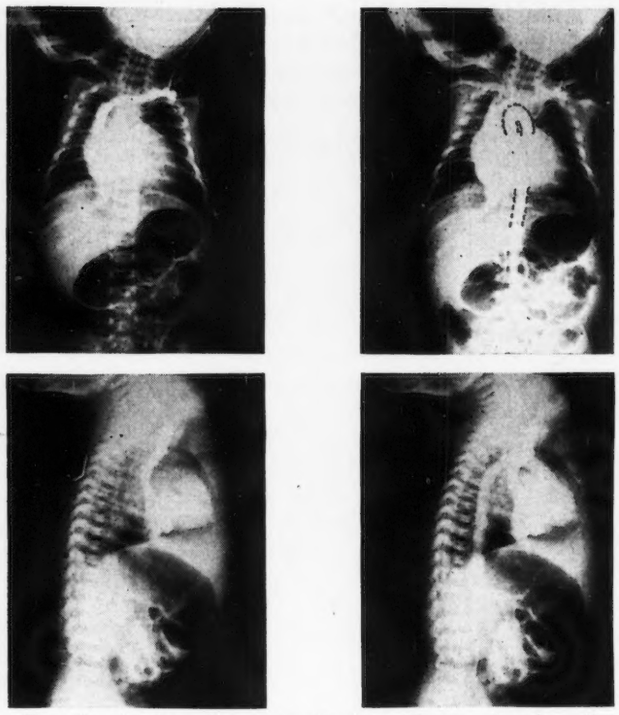

Fig. 2.—Angiocardiograms, in two planes, showing the aorta arising anteriorly from the right ventricle in transposition of the great vessels.

monary and systemic circulations. While this is a palliative procedure, the children operated upon are greatly improved and there seems to be no doubt that this is the best procedure available at the present time for the treatment of transposition.

As of April 1957, Baffes[10] reported that he had operated upon 38 patients, with 22 survivors in the immediate postoperative period. Thus the operative mortality has approximated 40%. However, when one considers that many of these infants were in severe difficulties, this mortality cannot be considered excessive. Four other of his patients have died after leaving hospital. Two of these died of infection, and two as a result of pulmonary arteriosclerosis. The remaining 18 survivors have all shown satisfactory clinical improvement, and their peripheral oxygen saturations have risen from preoperative levels of 35 to 50% to postoperative levels averaging 85 to 92%.

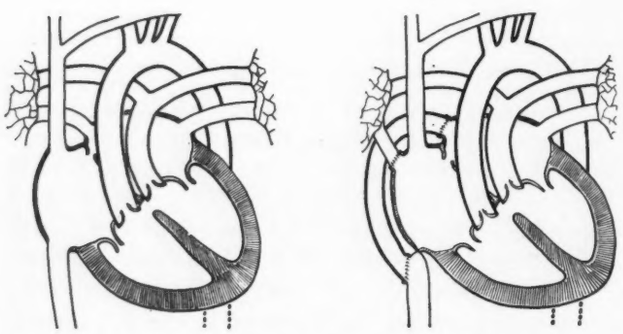

Fig. 3.—(a) Diagrammatic representation of transposition of the great vessels with patent foramen ovale and ventricular septal defect. (b) Diagram showing Baffes procedure. The inferior vena cava is ligated and blood is diverted to the left atrium through an arterial homograft. The right pulmonary veins are transposed from left atrium into right atrium.

Two children have been operated upon for transposition of the great vessels, employing the technique developed by Baffes, at the Winnipeg Children's Hospital. While this number is, of course, too small to warrant any conclusions, it was considered that this report might be of some value by emphasizing to physicians that transposition of the great vessels can no longer be considered a hopeless situation, and that an operation can be performed to help these severely crippled infants and children.

CASE REPORTS

CASE 1.—C.R., a baby girl, was born on March 27, 1957, following a normal pregnancy and delivery.

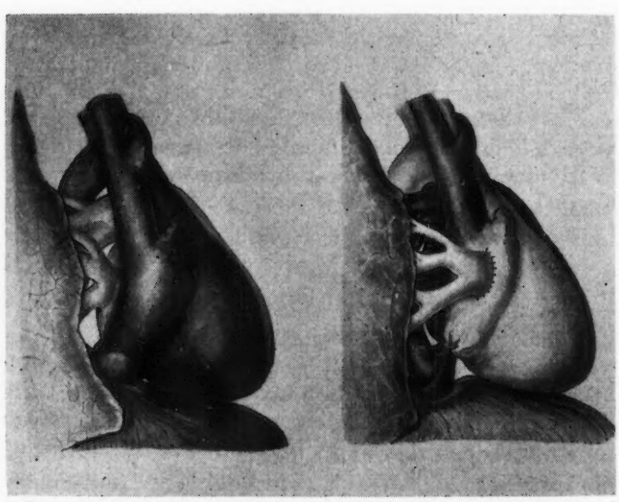

Fig. 4.—Drawings showing the operative appearance of transposition of the great vessels before and after the Baffes procedure. The only modification of the operation from that originally described by Baffes is purse-string ligation of the inferior vena cava instead of its division and suture.

Birth weight was 7 lb. 3½ oz. Very shortly after birth cyanosis appeared, and the child required oxygen therapy. A systolic murmur along the left sternal border was noted.

On May 3, 1957, the child was admitted to the Children's Hospital. Upon examination, she was found to be very cyanosed, but was quite vigorous and not in extreme distress. She weighed 8 lb. 9 oz. The heart was clinically enlarged. All peripheral pulses were present and were normal. A soft systolic murmur was heard along the left sternal border but there was not a palpable thrill. The liver edge was felt 2 cm. below the left costal margin.

The hæmoglobin value was 17.6 g. %. Electrocardiograms showed marked right ventricular hypertrophy. Heart fluoroscopy revealed the heart to be moderately enlarged, with a narrow cardiac waist. The pulmonary vascular markings were increased.

Angiocardiography was performed through the right external jugular vein. The aorta was visualized arising from the right ventricle, and in the lateral projection was seen to occupy an anterior position characteristic of transposition of the great vessels. The examination also suggested the presence of an atrial septal defect and a small patent ductus arteriosus. Because the baby, although markedly cyanosed, was doing moderately well, it was decided to defer any surgical attempt in the hope that this could be postponed until the child was older. Accordingly, the baby was discharged from hospital on May 7, 1957.

On August 31, 1957, at the age of five months, the baby was readmitted to hospital in heart failure. Despite all efforts to improve her condition, the child failed to respond. With full realization of the risks involved because of the infant's almost terminal state, the decision to operate on the child was made.

On September 4, 1957, through a right thoracotomy, the diagnosis of transposition of the great vessels was confirmed. Baffes' procedure was performed, using an arterial homograft to bridge the distance from the inferior vena cava to the left atrium. All anastomoses were accomplished without difficulty, and appeared to function well. The thoracotomy wound was closed with underwater chest catheter drainage.

Although we had not employed refrigeration, we purposefully kept the operating room cool, hoping to achieve a mild degree of hypothermia. At the conclusion of the operation, however, the baby's rectal temperature was down to 29° C. The child was rewarmed and although heart action was good and the infant's colour improved, respiration was slow and inadequate. Despite continued artificial pulmonary ventilation, the child did not improve and died seven hours after the operation.

Postmortem examination revealed a transposition of the great vessels, a patent ductus arteriosus with an internal diameter of only 1-1.5 mm. and a patent foramen ovale. The anastomoses of the graft to the inferior vena cava and to the left atrium were patent. The anastomosis of the right pulmonary veins to the right atrium was also adequate. Unfortunately, the child still had an anomalous right pulmonary vein which had been missed at the operation, and thus only a partial transfer of right pulmonary veins had been accomplished.

Death appeared to be due primarily to suppression of the respiratory centres, probably as a result of severe cerebral anoxia.

CASE 2.—This boy, K.H., was born on November 3, 1953, after a normal pregnancy and delivery. Cyanosis was present. Although the child's condition was sufficiently satisfactory to permit him to go home along with his mother, he continued to be blue and during the first few months of life had several anoxic episodes.

On February 21, 1955, at the age of 15 months, the child was admitted to the Winnipeg Children's Hospital. He was small and moderately cyanosed. Fingernails and toenails were clubbed. The heart was enlarged and a grade two systolic murmur was heard along the left sternal border, maximally in the fourth interspace. The liver was not enlarged. All peripheral pulses were normal.

The hæmoglobin value was 14.8 g. % and the hæmatocrit value 48%. Electrocardiograms showed right ventricular hypertrophy. Heart fluoroscopy revealed a large heart with prominent pulmonary vascular markings. An angiocardiogram established the diagnosis of transposition of the great vessels.

Because he was doing quite well, and because no method of successful surgical treatment was available at that time, the child was sent home.

On January 13, 1958, at the age of four years, the child was readmitted to hospital. In the interval since his previous admission, the boy had done moderately well, although his cyanosis had slightly increased. He tired easily on exertion, and for the last three months he had required to be digitalized because of mild cardiac failure.

On January 17, 1958, a Baffes procedure was performed. The rectal temperature was continuously recorded; during the five-hour procedure it dropped to 32° C. Continuous electrocardiography and electroencephalographic tracings showed no significant changes during the procedure.

The child's postoperative course was stormy, but he eventually improved and was discharged from hospital on the 18th postoperative day.

While a four-month follow-up is still too short to be significant, the child's colour is definitely improved (although he still becomes cyanosed on exertion) and his exercise tolerance is increased.

SUMMARY

Transposition of the great vessels occurs once in 11,000 births. It is the most common congenital heart lesion responsible for cyanosis appearing immediately after birth. The lesion carries with it a high mortality, and the vast majority of infants with the abnormality die before the age of six months.

The diagnosis can usually be suspected from the x-ray appearance of the heart and can be confirmed by angiocardiography.

The Baffes procedure, in which the inferior vena cava is transposed from the right atrium to the left, and the right pulmonary vein is transposed from the left atrium to the right, offers these children palliative improvement nearly equal to that obtained by the Blalock or Potts procedure in cases of tetralogy of Fallot.

The operation can best be accomplished in infants over six months of age but, because of the lethal nature of the lesion, must frequently be performed earlier in life.

The case reports of two children operated upon are included. The first infant, aged five months, was almost

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moribund before operation and died seven hours postoperatively. The second child, aged four years, has done well since his operation and shows marked clinical improvement.

I am indebted to Dr. Harry Medovy, Pædiatrician-in-Chief, Children's Hospital, Winnipeg, not only for his help in the preparation of this paper, but for his valuable consultative help in the management of these two patients.

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RÉSUMÉ

La transposition des grands vaisseaux s'observent une fois par onze mille naissances. Elle est la lésion cardiaque congénitale qui cause le plus fréquemment la cyanose que l'on voit immédiatement après la naissance. Elle comporte une mortalité élevée et la grande majorité des nourrissons qui sont affligés de cette anomalie meurent avant l'âge de six mois. On peut soupçonner sa présence d'après l'apparence radiologique du cœur; l'angiocardiographie en apporte la confirmation. Le procédé de Baffes par lequel la veine cave inférieure est transposée de l'oreillette droite à l'oreillette gauche, et la veine pulmonaire droite transposée de l'oreillette gauche à la droite, offre à ces enfants une amélioration palliative presqu'égale à celle que l'on obtient par les procédés de Blalock ou de Potts dans les cas de tétralogie de Fallot. L'opération se pratique dans les conditions les plus favorables chez les enfants âgés de plus de six mois, mais en vertu du danger que comporte la lésion on doit fréquemment intervenir avant cet âge. Les faits cliniques de deux enfants ayant subi cette opération sont rapportés. Le premier des deux, âgé de cinq mois, était presque moribond lorsqu'il fut opéré; il mourut sept heures après l'opération. Le deuxième enfant était âgé de quatre ans; il supporta bien l'opération et a montré depuis une amélioration clinique prononcée.

BLOOD COAGULATION IN SUBJECTS WITH AND WITHOUT CLINICAL EVIDENCE OF ATHEROSCLEROTIC VESSEL DISEASE

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THERE HAS BEEN increasing speculation about the possible association of atherosclerosis with increased blood coagulability. Recently, McDonald and Edgill[1] found that individuals with a history of ischæmic heart disease have what appears to be a hyperactive coagulation mechanism. During studies on the coagulation changes associated with alimentary lipæmia in subjects with and without clinical evidence of atherosclerotic vessel disease, the fasting values for various coagulation tests including some of those used by McDonald and Edgill[1] were determined. These results have been reviewed in order to see whether their findings could be confirmed for subjects with basilar, carotid, coronary and peripheral artery complications of atherosclerosis.

The coagulation studies carried out were: the whole blood clotting time in silicone-coated tubes, the platelet count, the Russell viper venom time and the activity of platelets, $Al(OH)_3$-treated plasma, serum, and plasma Christmas factor in thromboplastin generation. In addition, the fasting plasma density values were determined. The results from this investigation of 135 male subjects are presented in this communication.

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METHODS AND MATERIALS

Subjects:

Atherosclerotic.—The individuals with clinical evidence of atherosclerosis were those who had either proven atherosclerotic peripheral vascular disease, myocardial ischæmia or carotid or basilar artery stenosis. No subject was tested within five weeks of a known vascular accident.

Non-atherosclerotic.—These subjects had no clinical evidence of the disorders mentioned for the atherosclerotic group or of diabetes. This group of individuals was further divided on the basis of family history. If a subject's siblings, either parent, or siblings of either parent had a history of diabetes, peripheral vascular disease, myocardial ischæmia or a cerebrovascular accident under the age of 75, the subject was considered to have a positive family history. This was an arbitrary classification and some individuals were undoubtedly misclassified since the only proof of disease was the subject's statement.

COAGULATION STUDIES

The subjects ate nothing from 10:00 p.m. in the evening prior to the taking of the fasting blood sample in the morning. The coagulation tests were carried out as described previously,[2] with the following modifications. Thromboplastin generation test: A normal generation system was made up each day using freshly prepared normal $Al(OH)_3$-treated plasma, normal frozen serum, and brain extract. The $Al(OH)_3$-treated plasma, serum or platelets from each patient were then substituted for the corresponding material in the normal generation system and tested. The plasma activity was

TABLE I.—FASTING COAGULATION VALUES

Subjects		Age, years	Results of tests: Clotting time, minutes	Russell viper venom time, seconds	Platelet count No./c.mm.	Plasma optical density
Group A	Mean	38.7	25.7	13.2	244,800	0.0644
	S.D. ±	6.3	3.8	1.5	39,000	0.02
	S.E.	0.9	0.53	0.21	5,500	0.0028
Group B	Mean	37.1	25.8	13.7	222,700	0.058
	S.D. ±	7.7	3.4	1.2	43,500	0.022
	S.E.	1.1	0.51	0.17	6,400	0.0034
Group C	Mean	37.7	26.6	14.6	201,600	0.0486
	S.D. ±	11.7	3.5	1.2	39,200	0.02
	S.E.	1.9	0.57	0.19	6,400	0.0031
Probability of difference between means using T test	A & B p=		>0.05	>0.05	0.02	>0.05
	A & C p=		>0.05	0.001	0.001	0.001
	B & C p=		>0.05	0.01	0.05	>0.05

S.D. = Standard deviation. S.E. = Standard error.

assessed by diluting the plasma 1:10 with 0.85% saline and using it in place of serum in the normal generation mixture. Previously this activity was determined by mixing the dilute plasma with Christmas-factor serum and testing the change in activity of Christmas-factor serum. However, it was found that the degree of correction which plasma samples had on Christmas-factor serum was reflected in the activity of the plasma in the test system when no Christmas-factor serum was used.

PLASMA DENSITY

The fasting plasma density values were determined, using a Coleman junior spectrophotometer at 630 μ. The zero point was standardized by using distilled water.

RESULTS

For the purpose of comparison the subjects were divided into three groups:

A. Subjects with clinical evidence of atherosclerosis; 52 subjects.

B. Subjects with no clinical signs of atherosclerosis but a positive family history of atherosclerosis; 45 subjects.

C. Subjects with no atherosclerosis and an apparently negative family history; 38 subjects.

Whole blood clotting time.—There was no statistically significant difference between the mean values for the three groups of subjects (Table I).

Platelet count.—The mean platelet count was greatest for the subjects in group A and least for the subjects in group C. The difference between the means was significant, as was the difference between groups B and C, and A and B.

Russell viper venom time.—The mean value for subjects in group A was shortest and for subjects in group C longest. The difference between groups A and C was significant, as was the difference between groups B and C (Table I).

Plasma optical density.—The mean value for the subjects in group A was the greatest and those in group C the least. The difference was significant. The mean value for group B lay about half way between the values for groups A and C. The

TABLE II.—ACTIVITY OF $Al(OH)_3$-TREATED PLASMA IN THROMBOPLASTIN GENERATION TEST

Subjects		Incubation time in minutes: 1	2	3	4	5
		Clotting time in seconds				
Group A	Mean	42.4	16.4	11.8	11.2	11.2
	S.D. ±	19.1	10.3	3.0	1.3	1.5
	S.E.	2.65	1.43	0.42	0.18	0.21
Group B	Mean	47.0	22.2	12.5	11.3	11.1
	S.D. ±	16.6	14.5	5.7	1.7	1.3
	S.E.	2.5	2.2	0.9	0.25	0.2
Group C	Mean	47.4	20.3	12.7	11.9	12.0
	S.D. ±	16.3	12.6	2.2	1.4	1.3
	S.E.	2.65	2.05	0.36	0.21	0.21
Probability of the difference between the mean values using the T test	A & B p=			>0.05	>0.05	>0.05
	A & C p=			>0.05	0.02	0.01
	B & C p=			>0.05	>0.05	0.01

TABLE III.—ACTIVITY OF PLATELETS IN THROMBOPLASTIN GENERATION TEST

Subjects		Incubation time in minutes: 1	2	3	4	5
		Clotting time in seconds				
Group A	Mean	50.2	22.1	15.9	16.1	15.9
	S.D. ±	17.2	11.3	3.3	2.9	3.0
	S.E.	2.4	1.4	0.44	0.4	0.41
Group B	Mean	44.4	19.4	14.7	14.2	14.3
	S.D. ±	16.5	7.6	3.0	2.7	2.5
	S.E.	2.4	1.1	0.44	0.4	0.38
Group C	Mean	48.8	20.8	14.6	13.7	13.7
	S.D. ±	15.4	10.5	2.9	2.4	2.3
	S.E.	2.53	1.71	0.48	0.39	0.38
Probability of the difference between the mean values using the T test	A & B p=			0.05	0.01	0.01
	A & C p=			0.05	0.001	0.001
	B & C p=			>0.05	>0.05	>0.05

differences between these groups were not significant (Table I).

ACTIVITY OF FACTORS IN THROMBOPLASTIN GENERATION TEST

$Al(OH)_3$-treated plasma (factor V and AHG activity). – $Al(OH)_3$-treated plasma prepared from the subjects in groups A and B was slightly more active than $Al(OH)_3$-treated plasma prepared from group C. The mean values after four to five minutes' generation were significantly different for groups A and C. The differences between the mean values for groups B and C were significant at the fifth minute (Table II).

Platelet activity in thromboplastin generation test.—Significantly more thromboplastin was generated by the platelets prepared from subjects in groups B and C than by the platelets from subjects in group A after four and five minutes' incubation. There were no significant differences between the other groups (Table III).

Serum Christmas factor activity in thromboplastin generation test.—The serum prepared from the subjects in groups A and B was considerably more active in the thromboplastin generation test than that prepared from the subjects in group C. The difference between the mean values for these subjects was significant for the 3rd, 4th and 5th minutes of generation (Table IV).

Plasma Christmas-factor activity in the thromboplastin generation test.—The mean values for plasma samples from the subjects in groups A and B after four and five minutes of incubation were significantly greater than the mean values for subjects in group C. There was no significant difference between the values for the subjects in groups A and B (Table V).

DISCUSSION

The results for the control subjects without a family history of atherosclerosis and the atherosclerotic individuals are in agreement with those of McDonald and Edgill[1] as far as the fasting values for the whole blood clotting time and Russell viper venom time are concerned. In the present study, the mean platelet counts were found to be greater in the atherosclerotic group of subjects than

TABLE IV.—ACTIVITY OF SERUM IN THROMBOPLASTIN GENERATION TEST

Subjects		Incubation time in minutes: 1	2	3	4	5
		Clotting time in seconds				
Group A	Mean	44.7	17.3	13.1	11.5	11.7
	S.D. ±	17.6	8.6	3.6	1.9	2.7
	S.E.	2.4	1.2	0.5	0.26	0.38
Group B	Mean	46.5	24.1	13.1	11.5	11.5
	S.D. ±	17.7	12.5	4.4	1.6	1.5
	S.E.	2.6	1.9	0.66	0.24	0.2
Group C	Mean	48.1	25.2	15.5	14.3	14.1
	S.D. ±	15.7	15.6	4.5	3.6	2.9
	S.E.	2.58	2.55	0.74	0.59	0.47
Probability of the difference between the mean values using the T test	A & B p=			>0.05	>0.05	>0.05
	A & C p=			0.02	0.001	0.001
	B & C p=			0.02	0.001	0.001

TABLE V.—FASTING ACTIVITY OF PLASMA (CHRISTMAS FACTOR) IN THE THROMBOPLASTIN GENERATION TEST

		Incubation time in minutes				
		1	*2*	*3*	*4*	*5*
Subjects		*Clotting time in seconds*				
Group A	Mean	50.1	24.4	14.7	14.2	13.9
	S.D. ±	13.1	11.4	2.0	2.0	2.0
	S.E.	1.82	1.6	0.28	0.28	0.28
Group B	Mean	54.2	28.3	15.9	14.1	14.0
	S.D. ±	10.1	12.8	3.5	1.7	1.6
	S.E.	1.5	1.9	0.5	0.25	0.24
Group C	Mean	53.8	26.3	16.2	15.0	15.1
	S.D. ±	12.2	13.4	3.9	1.5	1.4
	S.E.	2.02	2.18	0.56	0.25	0.22
Probability of the difference between the mean values using the T test	A & B p=			0.05	>0.05	>0.05
	A & C p=			0.05	0.05	0.01
	B & C p=			>0.05	0.02	0.01

in the non-atherosclerotic subjects. McDonald and Edgill[1] found no difference in this regard between the subjects with ischæmic heart disease and the control group. They reported that the combined activity in the thromboplastin generation test of $Al(OH)_3$-treated plasma and serum from the coronary patients was greater than for the controls. In the present study it was found that both the $Al(OH)_3$-treated plasma and serum tested separately had more activity than for the controls with a negative family history. The difference was more marked for the serum. On the basis of McDonald and Edgill's results and the findings in this study, it is possible to conclude that subjects with a history of myocardial ischæmia and other clinical manifestations of atherosclerosis may have a more active coagulation mechanism than individuals with a negative family history and no clinical evidence of atherosclerotic vascular disease.

The activity of the platelets in the thromboplastin generation test was not entirely in keeping with the results for the other tests. The platelets from the non-atherosclerotic subjects appeared to be the most active in thromboplastin generation. In the case of the atherosclerotic subjects and the control group with the negative history, the difference was significant. This could be used as an argument against the hypothesis that the clotting mechanism is more active in atherosclerotic subjects. Preliminary studies suggest that the less active platelets fail to disintegrate readily or release the platelet factor necessary for thromboplastin formation.

The plasma (Christmas factor) activity was significantly greater in the atherosclerotic subjects than in the control subjects with a negative family history, and the difference between the controls with a positive family history and those with a negative family history was also significant. This test system has been found active in disorders where blood clotting occurs. This finding further supports the hypothesis that atherosclerotic individuals have a more active coagulation mechanism.

Individuals with a positive family history of atherosclerosis but no clinical evidence of the disease had values similar to the atherosclerotic subjects for most tests. Indeed, the activity of $Al(OH)_3$-treated plasma, serum and plasma (Christmas factor) in the thromboplastin generation test for this group of subjects was significantly greater than for subjects with a negative family history. The findings for the two non-atherosclerotic groups suggest that subjects with a family history of atherosclerosis have a more active clotting mechanism than subjects with a negative family history. Although it is not known whether the hypercoagulable state is a result rather than a cause of the clinical complications of atherosclerosis, this observation suggests that increased blood coagulability may be an etiologic factor.

SUMMARY

The state of the blood coagulation mechanism was studied in 135 fasting male subjects with and without clinical atherosclerosis. A statistically significant difference was found between the subjects with clinical manifestation of atherosclerosis and the control group with a negative family history, in respect to the Russell viper venom time and the activity of serum, $Al(OH)_3$-treated plasma, and plasma (Christmas factor) in the thromboplastin generation test. The difference between the platelet counts was also found to be significant between these two groups. The mean values for the Russell viper venom time, the platelet count and the mean activity in the thromboplastin generation test of $Al(OH)_3$-treated plasma, serum and plasma (Christmas factor) prepared from subjects with no clinical evidence of atherosclerosis but a positive family history was significantly greater on a statistical basis than for the control subjects with a negative family history for atherosclerosis. This evidence suggests that subjects with clinical evidence of atherosclerosis have hypercoagulability of the blood and that subjects who are prone to this disease (i.e., a positive family history) have increased coagulability of the blood before the development of clinical complications.

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RÉSUMÉ

L'auteur a comparé l'état des mécanismes de coagulation chez 135 hommes à jeun tant normaux qu'artérioscléreux. Il observa une différence importante au point de vue statistique entre les deux groupes dans le temps de réaction au venin de vipère Russell, et dans l'épreuve de production de thromboplastine, par le sérum, le plasma traité à l'hydroxyde d'aluminium et le facteur Christmas. Il existait aussi une différence importante dans le nombre des plaquettes des deux groupes. Les résultats de toutes ces épreuves chez les sujets cliniquement libres d'atteintes artérioscléreuses mais dont les antécédents indiquaient une tendance dans ce sens, accusèrent une différence statistique appréciable comparés aux sujets dont le système vasculaire des ascendants était sain. Ce travail semblerait indiquer que les sujets montrant des signes cliniques d'artériosclérose manifestent une hypercoagulabilité du sang alors que ceux apparemment normaux mais de souches artérioscléreuses ont une coagulabilité exagérée avant de montrer les complications cliniques de ces troubles.

Case Reports

INTRAVENOUS POLYETHYLENE CATHETER SUCCESSFULLY REMOVED FROM THE HEART*

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MOST CARDIAC FOREIGN BODIES are penetrating missiles which reach the heart by direct trauma. However, there have been described in the literature[1] a small number of cases in which the foreign body entered the cardiac chamber in an embolic fashion by way of the venous system. Again, most of these were fragments of metal, the result of traumatic penetration of a distant site.

Turner and Sommers[2] reported the accidental passage of a fine polyethylene catheter, 22 cm. in length, from a right cubital vein to the right atrium of a 250-lb., 54-year-old female. The catheter, which was being utilized for intravenous administration in a seriously ill patient, disappeared during an episode of restlessness and was found post mortem, two days later, in the right atrium and superior vena cava. The following is a report of a somewhat similar case in which the polyethylene catheter was successfully removed.

E.W., a 10-year-old white girl, was admitted to her community hospital on January 2, 1958, with acute appendicitis. Through a McBurney incision, a perforated, acutely inflamed appendix was removed. While she was in the operating room, an 18-cm. length of fine polyethylene tubing (PE50, 0.58 mm. I.D., 0.965 mm. O.D.) was threaded into the median cubital vein at the left elbow for intravenous infusion. This was carried out through a large needle stab and after the needle was removed, the tubing was taped, without looping, in line with its vein. Shortly after her return to the ward, the patient became quite restless. The intravenous connections separated and the polyethylene tubing disappeared. Fluoroscopy at this time suggested that the tubing was still lodged in the left brachial vein; however, when the brachial and axillary veins were exposed through separate small incisions, the tubing was not found. Chest roentgenograms did not reveal its location.

On January 9, 1958, seven days after her appendectomy, the patient was transferred to the Hospital for Sick Children, Toronto. At that time, her general condition was good. Pulse 120, regular, blood pressure 105/70 mm. Hg. She was on antibiotic therapy, and the moderate discharge from her abdominal incision grew *Streptococcus viridans.* Her pulmonary second sound was normal and there were no heart murmurs. A tiny needle puncture wound could still be seen over the left median cubital vein. There was a small incision over the left brachial vein and another over the lower portion of the left axillary vein. Electrocardiograms were normal and chest roentgenograms including tomograms showed no evidence of the polyethylene tube.

While her wound closed completely, the patient was carefully followed clinically and radiologically for some sign of the polyethylene catheter. Repeated chest films were taken to detect any suggestion of the tubing in the pulmonary vascular bed. On January 27, 1958, with the belief that the foreign body must, by exclusion, be in or about the heart, an exploratory operation was carried out. Hypothermia to 31° C. (rectal) was used to permit inflow stasis and exploration of the right atrium or pulmonary artery, if necessary. Through a midline sternal splitting incision, avoiding both pleural spaces, the pericardium was incised anteriorly.

Externally, the heart appeared normal. Palpation of the main pulmonary artery failed to disclose the tubing but on enlarging the pericardial incision it could be felt easily within the superior vena cava. Where it entered the right atrium, this vessel showed some moderate reaction with thickening of its wall. The segment of the superior vena cava within the pericardium was isolated between two umbilical tape tourniquets, one at the junction with the right atrium, just below the right pulmonary artery, and the other at a level just above the right pulmonary artery. Through a longitudinal incision in this segment of the superior vena cava the polyethylene tubing was grasped at what proved to be its midpoint and withdrawn from the superior vena cava and right atrium. There was no apparent thrombus on the tubing but this could have been brushed off in removal. Flow was established by releasing the caval tapes after clamping

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the cut edges of the caval incision with a Potts coarctation clamp. The superior vena cava had been completely obstructed for five minutes. The short incision was sutured with 5-0 arterial silk and then the clamp removed.

Postoperative care included superior mediastinal drainage, moist oxygen and antibiotics. Her progress was smooth and she was allowed up on the fourth day and home on the 13th day. For several days, just before discharge, minimal jugular venous distension was noted. However, when she was seen twelve weeks later this was not evident and she was in reasonable health.

DISCUSSION

Various authors[3, 4] have discussed the indications for removal of cardiac foreign bodies. These indications vary for the size, nature and exact site of the foreign body and are mainly concerned with the prevention or treatment of such complications as: thrombosis, embolism, myocardial damage, bacterial endocarditis, recurrent pericardial effusions, psychoneurosis and coronary vessel damage. In Turner and Sommers's case, where the end of the polyethylene catheter contacted the right atrial wall, there developed a patch of myocardial necrosis and mural thrombus 2 cm. in diameter. As well, the catheter was surrounded by a thin layer of ante-mortem blood clot. Indeed, the entire right side of the heart was said to be filled with similar material. Obviously, the possibility of these complications necessitates removal of such a foreign body. In the case reported here, the only apparent effect was moderate inflammatory reaction with thickening of the superior vena caval wall at its junction with the right atrium. Postoperatively, the patient developed transient, mild jugular venous distension. This was considered due to narrowing of the superior vena cava. Consequently, we believe that such a foreign body should be removed as soon as diagnosis and the patient's condition permit. Also, because of the danger of further narrowing the superior vena cava by suturing, it would seem safer to remove the cannula through an incision in the right atrium, particularly in this case where the vessel was already involved in an inflammatory reaction.

Before surgery, one would prefer to know the exact site of the foreign body. This was not determined here, the site of the tubing being assumed by deduction. Angiocardiography was not considered worth while but, in certain other situations, this procedure might well be helpful. It is significant that in both these cases, the fine, flexible polyethylene catheters failed to enter the right ventricle but remained in the right atrium and superior vena cava.

As shown in Fig. 1, the leading end of the polyethylene tube probably came to lie against the right atrial wall adjacent to the tricuspid valve. Blood flow would discourage passage of the tubing into the inferior vena cava. The angle and position of the tricuspid valve orifice would make it difficult

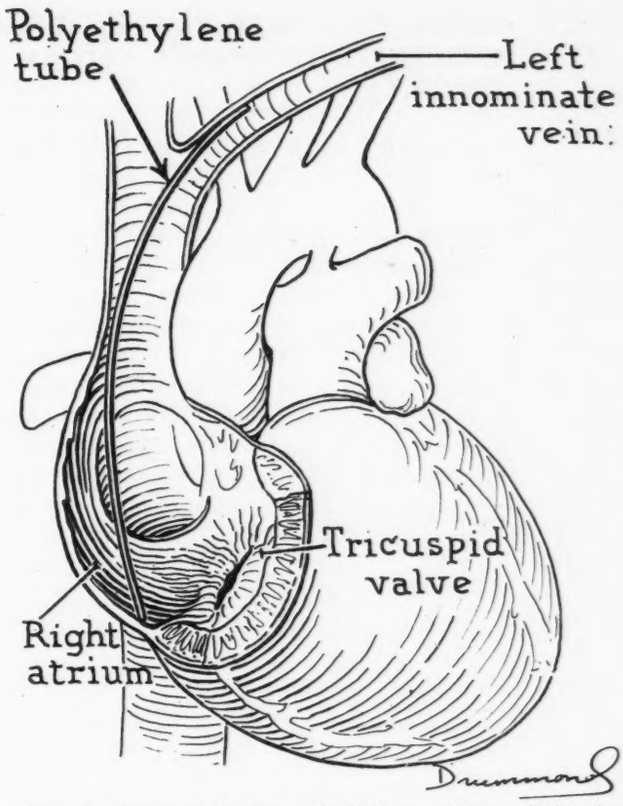

Fig. 1.—Position of the polyethylene tubing within the right atrium and superior vena cava.

for a straight catheter to enter the right ventricle, particularly if one end was still in the innominate vein. However, even if it did, it would not likely manœuvre distally into the pulmonary artery, and therefore could still be retrieved through the right atrium.

It may seem superfluous to emphasize the need for care in the intravenous use of small polyethylene cannulæ. On the other hand, it is likely that in the past this complication has occurred more frequently than generally recognized. In the future, with increasing use of plastic tubing it will no doubt occur again. Particularly dangerous is the insertion of very small tubing through a needle stab into a large vein. This very useful technique can be made safe by looping the tubing and securing it directly with tape or suture.

SUMMARY

A case is reported in which an 18-cm. length of fine polyethylene tubing passed in embolic fashion from a left cubital vein to the right atrium and superior vena cava of a 10-year-old child. It was successfully removed through a small incision in the superior vena cava.

The need for early removal of such a foreign body is briefly discussed and its likely position mentioned.

Acknowledgment is made to Dr. John Keith for assistance and guidance in the handling of this case.

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AORTIC VALVULAR INSUFFICIENCY ASSOCIATED WITH RHEUMATOID ARTHRITIS*

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THE FOLLOWING CASE REPORT is considered of interest for three reasons: (1) it describes the occurrence of acute rheumatic fever, rheumatoid spondylitis, and rheumatoid arthritis in the same individual; (2) it demonstrates that aortic valvular insufficiency may be tolerated for 23 years; and (3) it illustrates the uncommon clinical syndrome of chronic rheumatoid disease, delayed conduction of the stimulus to cardiac contraction, and severe aortic valvular insufficiency in association with the pathological findings of aortitis and aortic valvular endocarditis.

Clinical Findings

In 1916, an 18-year-old, white, Canadian-born soldier developed fever in association with acutely painful swollen hot ankles. His illness was diagnosed as acute rheumatic fever. His symptoms cleared in two weeks without apparent residual effects. Following this, he had frequent sore throats attributed to recurrent tonsillitis. For this reason, his tonsils were removed in 1919. Through the 1920's, he had intermittent lumbar backache and stiffness. In 1925, he was said to have a sacroiliac subluxation. By 1930, he had a "poker spine". In 1935, an aortic diastolic murmur was first recorded.

In the years between 1935 and 1946, he had almost continuous inflammatory involvement of the peripheral joints. An attempt at gold therapy in 1938 was discontinued because of the development of a skin rash. In 1945, he went to bed, never to be up again. In bed, his peripheral joints became fused.

In 1947, he developed severe bilateral iritis. With the formation of secondary cataracts, he became totally blind.

Symptoms of left ventricular failure began in 1957. In the month before his death in 1958, the following observations were made: bilateral cataracts; total spinal fusion; slight mobility in the shoulders; "opera-glass" hands; subluxations of the toe joints; fusion of the remaining peripheral joints; shaking of his whole body and bed with each heart beat; aortic diastolic murmur grade iv (out of vi) in intensity; grade iii precordial systolic murmur; blood pressure 160/50 mm. Hg; Corrigan pulse; "pistol-shot" sounds over the femoral arteries; increasing pulmonary congestion; hæmoglobin level 9.6 g. % per 100 ml.; red cell count 3.5 million per c.mm.; hæmatocrit 33%; sedimentation rate 58 mm. in one hour (Wintrobe method, not corrected for anæmia); electrocardiographic pattern of left ventricular hypertrophy; PR interval 0.24 second (Fig. 1). Repeated serologic tests for syphilis at irregular intervals throughout his illness were negative.

Gross Pathological Findings

The locomotor and cardiorespiratory symptoms were of particular interest. (The eyes were not examined.)

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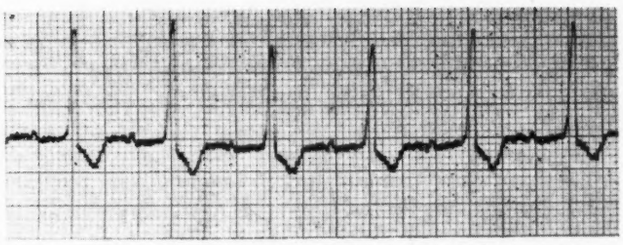

Fig. 1.—Electrocardiogram: standard lead I. The PR interval is 0.24 second in duration; the RST segment is depressed; the T wave is sharply inverted. These findings were interpreted to indicate delayed atrioventricular conduction and left ventricular hypertrophy. The patient was taking digitalis in small doses at the time the tracing was made.

The entire spinal column was fixed in a shallow curve (convex posteriorly). There was slight mobility at both shoulders; the joints of the fingers and toes were flail joints. The other peripheral joints were fused.

The heart was massively enlarged, weighing 1060 grams; this enlargement was due to hypertrophy of the left ventricular myocardium, the anterolateral wall measuring more than 2.5 cm. in thickness at some sites. The left ventricular cavity was monstrously dilated. The chambers and valves on the right side of the heart were normal. The left atrium was slightly dilated; the annulus of the mitral valve was also dilated, permitting mitral valvular insufficiency. The leaflets of the mitral valve were thin and felt normal in consistency; the chordæ tendinæ were normal. The annulus of the aortic valve and the ascending aorta were dilated. The commissures of the aortic valve were separated; the cusps of the aortic valve were thickened and contained palpable plaques of calcium at their bases; the free edges of the cusps were rolled and retracted.

There were large bilateral pleural effusions. The lungs were œdematous.

Histological Findings

Microscopic examination of the left ventricular myocardium showed no evidence of active or healed Aschoff nodules. Patchy areas of myocardium showed ischæmic changes. Focal collections of lymphocytes were present in the basal portions of the mitral valve leaflets.

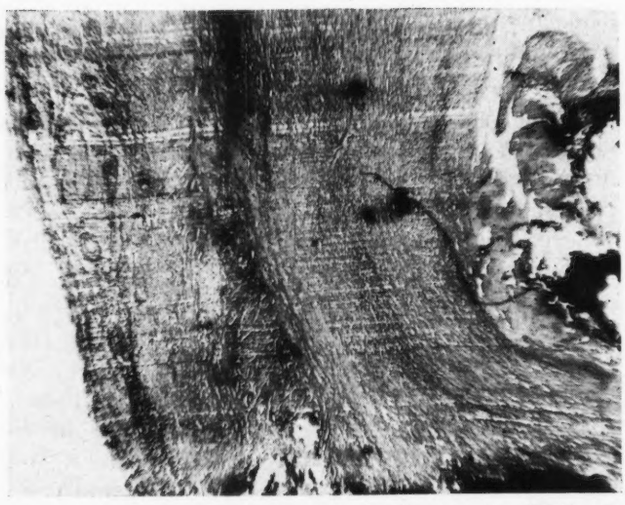

Fig. 2.—Photomicrograph of ascending aorta (Mallory's stain for elastic fibres). The right coronary cusp of the aortic valve appears on the right. Note the thickened rolled free edge of the cusp and the fragmented calcific deposits at the base of the cusp. The elastic fibres in the root of the aorta are few in number and disorganized in pattern.

Sections through the aortic valve and aortic valve ring showed the presence of interwoven bundles of hyalinized connective tissue in the free edge of the cusps. Towards the basal portions of the valve cusps, in addition to this hyaline degeneration, well-defined calcific deposits were present. In relation to these deposits, there were focal collections of lymphocytes and plasma cells showing no particular evidence of perivascular arrangement.

Elastic-tissue stains revealed a rather marked fragmentation and loss of elastic fibres at the base of the aortic valve and in the first portion of the ascending aorta (Fig. 2). The small vessels in the adventitia had thickened walls and narrowed lumina; this thickening appeared due to subintimal hyaline deposition rather than to endothelial proliferation.

DISCUSSION

The "rheumatic" diseases are not merely arthritides but systemic diseases. Cardiovascular involvement in the "rheumatic" patient, then, should not be considered a complication, but should be regarded as an integral part of the disease. For reasons that are presently obscure, clinically significant cardiovascular involvement in rheumatoid arthritis and spondylitis is uncommon. However, a small number of cases have been reported establishing a syndrome of severe aortic valvular insufficiency related to pathologically demonstrable aortitis and aortic valvular endocarditis in rheumatoid disease.

One of the earliest cases of this syndrome to be reported was presented at the weekly clinicopathological conferences[1] at the Massachusetts General Hospital in 1936. The patient was a young man (26 years old at the time of his death) with typical peripheral rheumatoid arthritis. He was anæmic and had an elevated sedimentation rate. His electrocardiogram showed left bundle branch block. He had advanced aortic valvular insufficiency and left ventricular failure. Postmortem examination revealed an active aortitis and aortic valvulitis.

By 1951, Walter Bauer and his associates[2] at the Massachusetts General Hospital felt that they had accumulated sufficient data "to conclude that aortitis and aortic endocarditis do occur as a manifestation of rheumatoid arthritis. The clinical and pathological features of this type of heart disease are sufficiently distinctive to exclude syphilis and rheumatic fever as etiological agents."

Recently, Schilder, Harvey and Hufnagel,[3] at Georgetown University, after evaluating 100 patients with aortic insufficiency for possible surgical treatment, collected a series of 6 cases (5 in the body of their report, one in an addendum) with certain common clinical features: (1) long-standing rheumatoid spondylitis; (2) elevation of the sedimentation rate; (3) anæmia; (4) severe aortic valvular insufficiency; (5) radiological and electrocardiographic evidence of left ventricular hypertrophy; (6) prolonged atrioventricular conduction; and (7) negative serologic tests for syphilis. In the two of their cases in which pathologic data were presented, there was aortic valvulitis. In the one case in which the root of the aorta was examined microscopically, "all the layers were greatly scarred and thickened by hyalinized fibrous tissue".

The total number of similar cases with both clinical and pathological documentation reported in the medical literature is small. This probably reflects the true rarity of this syndrome, for a large number of intensive investigations[4] of patients with rheumatoid disease have indicated a low incidence of clinically significant heart disease.

The patient described in this case report demonstrated all the clinical and pathological features of this syndrome of rheumatoid aortic valvulitis. His skeleton was almost totally fused. He was anæmic and had an elevated sedimentation rate. Repeated serological tests for syphilis were negative. He had the central and peripheral signs of severe aortic valvular insufficiency. It is interesting that, although this aortic insufficiency was tolerated for 23 years, it eventually resulted in his death. His electrocardiogram revealed first-degree heart block. The pathological findings indicated a long-standing aortic valvulitis and aortitis. Dilatation and hypertrophy of the left ventricle were marked. The aortic valve was incompetent because of separation of the commissures and retraction of the free edges of the valve cusps. Valaitis, Pilz and Montgomery[5] ascribe the deformities of the aorta and aortic valve to fibrosis of necrobiotic rheumatoid lesions. Microscopic examination showed that the inflammatory reaction was much less acute than that described in the early case[1] observed at the Massachusetts General Hospital (the total duration of that patient's illness was approximately seven years), but was similar to that observed in the second case reported by Schilder *et al.*[3] (the total duration of that patient's illness was 10 to 20 years). In these three cases (M.G.H., 1936;[1] Schilder *et al.*, 1956;[3] and Bowers, 1958), the absence of Aschoff bodies has been specifically emphasized.

The clinical picture and the pathological findings in the case reported in this paper lend confirmation to the conclusions clearly stated by Bauer and his associates[2] that aortitis and aortic endocarditis do occur as a manifestation of rheumatoid disease, and that this form of heart disease is a specific entity distinct from rheumatic and luetic heart disease.

SUMMARY

The case history of a patient with total skeletal fixation due to rheumatoid arthritis, total blindness due to bilateral iritis with secondary cataracts, and fatal aortic valvular insufficiency is presented in detail. It is suggested that the aortic valvular insufficiency was caused by a specific form of aortitis and aortic valvular endocarditis distinct from that occurring in rheumatic and luetic heart disease.

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BASILAR ARTERY OCCLUSION
REPORT OF A CASE WITH TEN YEARS' SURVIVAL

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THROMBOSIS of the basilar artery is regarded as a rare and difficult clinical diagnosis, and although the majority of cases result in a fatal outcome, recoveries have been reported, as for example by Freeman and Ellis.[1]

The first recorded case of basilar artery occlusion was by Hayem[2] in 1868, and seven years later Leyden[3] published a report of two cases of basilar artery thrombosis from syphilitic endarteritis. In 1946, Kubik and Adams[4] made a survey of the incidence of basilar artery occlusion and found 13 cases in 4200 consecutive autopsies at the Massachusetts General Hospital, and a further 12 cases among 3200 consecutive autopsies at the Boston General Hospital, making a median average of 1:300 autopsies. Of these 25 cases no clinical data were available in 7, and of the remaining 18 the occlusion was found to be due to thrombosis in 11 and to embolism in 7. Survival following complete occlusion of the basilar artery either by disease[5, 6] or by surgical ligation[7] has been reported in the literature. Survival is attributed to the effectiveness of anastomotic connections between the cerebral arteries which permit bypass of the block in the basilar artery. Extensive communications between the middle and posterior cerebral artery and among the long cerebellar vessels have been described.[6-9]

SIGNS AND SYMPTOMS

The clinical signs and symptoms of basilar artery occlusion are typical, and diagnosis should be possible in the majority of cases. The principal features are the sudden onset with initial symptoms of headache, dizziness, disorientation and coma. Temporary improvement is common but in the majority of cases death occurs within 2 to 30 days. Other characteristic features which may be present in varying degrees are:

1. Dysarthria and unilateral paræsthesia.
2. Facial palsy.
3. Hemiplegia or quadriplegia with bilateral plantar extensor reflexes.
4. Pupillary abnormalities and disorders of ocular movements.
5. Normal cerebrospinal fluid.

This is a case report of a patient who survived for ten years following basilar artery occlusion.

The patient, a married white male aged 42 years, was admitted to Bridgeport Hospital, Bridgeport, Connecticut, on June 6, 1955. He gave a history of an episode of left-sided paralysis occurring ten years earlier and accompanied by diplopia, difficulty in swallowing and dysarthria. During this period he was treated at home by his family physician, and his condition improved rapidly so that by the seventh day he had no apparent residual disability. No definite diagnosis was made at that time. He remained in good health for the next ten years, except for regular episodes of impairment of consciousness occurring approximately every six months, for which he did not seek medical advice.

On his final admission he gave a history of left hemiplegia of three days' duration and sudden onset.

Physical Examination

The patient was well nourished and well developed, conscious and co-operative. There was complete paralysis of the left arm and left leg, and slight weakness of the left side of the mouth. The left pupil was larger than the right pupil and did not react to light. The left eye tended to deviate to the left and there was nystagmus of the left eye only on left lateral gaze. Movements of the left eye were possible in all directions but medial movement was weak. The right eye could be moved up and down normally but could not be moved either medially or laterally. Speech was dysarthric and co-ordination could not be tested. Over the next eight days his condition improved slightly with the return of some weak function in his left arm and leg and return of normal speech. On the ninth day the patient developed peripheral vascular collapse from which he slowly recovered, but without any alteration in his neurological status. After this he made a gradual but progressive recovery and on the 17th day after admission he was discharged to a nursing home; there was only moderate function in his left side but he was able to walk with the assistance of a "walker". Automatic bladder function was present. The condition was diagnosed at that time as an acute episode of multiple sclerosis.

Readmission

On August 15, 1955, the patient was readmitted with an acute recurrence. This time he was completely unable to move his body or his extremities or any muscles supplied by his cranial nerves and could make only inarticulate vocal sounds. He was capable of understanding to some degree when spoken to, but unable to carry out requested movements. Deviation of the head to the right was present; pupils

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were central and equal and reacted normally to light and accommodation. The optic discs were normal. It was impossible to determine the status of the other cranial nerves but oculomotor paralysis was present and it was apparent that the medullary centres for swallowing, speech and respiration were affected. Left spastic and right flaccid paralysis of the extremities was present with bilateral plantar extensor reflexes. The other reflexes were present bilaterally but increased on the left side.

Progress

Tube feeding and intravenous therapy were carried out, and over the next three days his general condition showed marked improvement with the return of voluntary movement in both upper extremities. On the fourth day the patient suddenly developed extreme respiratory distress of central origin and was placed in a respirator. After three days in the respirator he was found to have regained his normal respiratory function and was removed from the respirator. At this stage, despite antibiotic therapy and completely negative findings he developed a fluctuant pyrexia of 101° F. to 104° F. His general condition remained unchanged, he never regained any further function, and on September 23, 1955, he suddenly developed a temperature of 106° F., became comatose and died.

Laboratory Examinations

Examination of spinal fluid on both admissions failed to reveal any abnormality. The initial spinal fluid pressure was 145 mm. and the final pressure after spinal tap was 110 mm. The cerebrospinal fluid was clear and colourless. One lymphocyte per c.mm. was present. Pandy reaction was negative. The protein level was 20 mg. %; sugar 146 mg. %, chlorides 122 mEq./l. On all admissions his hæmoglobin level was 13.1 g. %, and the hæmatocrit 44%. On his first admission he had a white cell count of 33,800 (neutrophils 81%, lymphocytes 14%), and on his subsequent admission this had dropped to 13,300 (neutrophils 62%, lymphocytes 26%). Blood chemical findings were within normal limits during the whole time and his blood urea nitrogen never exceeded 23 mg. %. Urine was essentially normal except for minimal albuminuria and in the terminal stages where a urinary tract infection developed with *Pseudomonas æruginosa*. Blood and spinal fluid cultures were negative at all times.

Necropsy Examination (autopsy performed 4 hours after death):

Thorax: The lungs were of normal size and weight. Cross sections revealed no œdema or congestion. The heart was of the normal globular shape and weighed 340 grams. The pericardial sac had a smooth lining and contained 15 ml. of clear, straw-coloured fluid. The auricles contained a small amount of post-mortem thrombus. The tricuspid and mitral valves admitted respectively the tips of three and two fingers. The pulmonary and aortic valves were normal. All valve cusps were normal. Multiple cross sections of the myocardium showed the usual homogenous reddish-brown parenchyma with a moderate amount of greyish streaking which was most pronounced on the posterior aspect of the left ventricle. The aortic arch and the thoracic aorta showed minimal atherosclerosis, but the abdominal aorta showed marked ulcerative atherosclerosis. Examination of the common iliac arteries also showed ulcerative atherosclerosis.

Abdomen: The liver appeared to be moderately congested. The spleen, pancreas and kidneys appeared normal. An adenoma was present in each adrenal gland and measured 1 cm. in diameter.

Brain: Examination of the brain after formalin fixation revealed the normal sulcal and gyral pattern. The meninges were normal. The vessels of the circle of Willis showed marked patchy atherosclerosis throughout, while the basilar artery was completely occluded by yellowish-grey atheroma firmly adherent to the vessel wall. The vertebral arteries were patent and showed only minimal atherosclerosis. An area of pontine infarction measuring 1 cm. in diameter was present. There was no gross hæmorrhage. Sections through the cortex, midbrain and cerebellum revealed no abnormality.

MICROSCOPICAL EXAMINATION

Heart: The heart showed extensive and irregular fibrotic scars which separated the myocardial fibres by dense fibrous tissue. There was no evidence of recent infarction. The coronary arteries showed minimal intimal fibrous thickening.

Lungs: The alveolar walls of the lungs were considerably thickened by fibrosis, and many small areas of atelectasis were present. There was no evidence of pneumonia or œdema.

Liver: The liver showed centrilobular congestion and some of the liver cells showed necrosis while others contained hæmosiderin. There was no fibrosis.

Adrenals: The presence of bilateral adrenal cortical adenomata was confirmed.

Brain: Sections of the cerebral cortex showed moderate œdema. The pons contained many small areas of infarction. Large numbers of Gitter cells were present in these areas. Minimal lymphocytic infiltration was present in the Virchow-Robin spaces adjacent to the areas of pontine infarction. There was no evidence of multiple sclerosis.

Basilar artery: Sections of basilar artery showed complete occlusion extending for a length of 2 cm. The occlusion was due to a well-organized thrombus, with old fibrosis and containing cholesterol deposits. One area of the thrombus showed a microscopic attempt at recanalization. At other levels in the basilar artery the intima was extremely thickened, with cholesterol deposits and fibrosis.

Spinal cord: Sections revealed no abnormality or evidence of multiple sclerosis. Death was attributed to basilar artery occlusion with pontine infarction.

CONCLUSION

The only significant cerebral finding at autopsy was the presence of a 2 cm. long area of occlusion of the basilar artery. The effectiveness of anastomotic connections between the cerebral arteries and also the long cerebellar vessels has already been mentioned, and it appears that in this case the cerebral circulation was thus adequately maintained over the ten years after his basilar artery occlusion. As no other lesion was present to account for his symptoms over the previous ten years, we must assume that these were due to a fall in the

cerebral blood flow to below critical levels. This was probably due to systemic effects, especially a fall in the systemic blood pressure, and although no definite evidence of recent myocardial infarction could be found, the presence of extensive old myocardial fibrosis would indicate that previous episodes of myocardial infarction with a fall in systemic blood pressure had occurred. Furthermore we must assume that a terminal myocardial infarction occurred, with again a reduction of cerebral blood flow to below critical levels, especially in that area which had little or no reserve capacity above the minimum required, and thus infarction of the pons took place with death of the patient.

SUMMARY

The neurological signs and symptoms of basilar artery occlusion are described. A case of ten years' survival after occlusion of the basilar artery is reported.

Death was ultimately due to a fall in systemic blood pressure, following a probable myocardial infarction resulting in a reduction of cerebral blood flow to below critical levels, especially in the area of the pons where the reserve capacity was minimal because of prior occlusion of the basilar artery.

The author is indebted to Dr. Russel Pope of Bridgeport Hospital, Bridgeport, Connecticut, for his advice and assistance.

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ŒSOPHAGOBRONCHIAL FISTULA COMPLICATING ŒSOPHAGEAL DIVERTICULUM*

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ŒSOPHAGOBRONCHIAL FISTULA may arise as a complication of either neoplastic or non-neoplastic conditions. Those arising as a complication of malignant lesions of either the respiratory or the digestive passages represent a well-known entity. Clerf[1] reviewed all the cases of œsophagobronchial fistula up to 1943 and found 610 cases. Coleman and Bunch reviewed an additional 75 cases in 1950,[2] and in 1956 Duprez, Wittek and Dumont[3] 10 more cases. Monserrat classified his cases from an etiological standpoint, and observed that 367 were neoplastic, 222 congenital, 41 infectious, and 40 traumatic. Coleman and Bunch found their series to be 28% traumatic in origin, 19% due to specific infection, 15% secondary to an œsophageal diverticulum, and the remainder neoplastic or congenital.

Œsophagobronchial fistula is the least frequent of all abnormal communications between the respiratory and digestive tracts, accounting for about one-third of all cases, while œsophagotracheal fistula makes up the other two-thirds. This latter type is usually congenital and associated with atresia of the œsophagus. According to Duprez[3] œsophagotracheal fistulæ are usually diagnosed and treated early in life, while œsophagobronchial fistulæ occur in adult life. Non-neoplastic œsophagobronchial fistulæ can result from congenital diverticula, or from acquired diverticulum secondary to trauma; theoretically then any diverticulum, of either the tracheobronchial tree or the œsophagus, can form a fistulous opening into its opposite member when inflammation occurs. The non-neoplastic type of œsophagobronchial fistula is less common and presents many difficulties in diagnosis. It is the object of this report to describe a case illustrating some of the aspects of this variety.

A 53-year-old white man was admitted for the first time because of an episode of passing blood by mouth.

For a period of approximately two years he had had episodes during which he noted that his sputum was bloodstreaked and that after these episodes his stools were black in colour. These episodes occurred once or twice a month and were not accompanied by any other symptoms, and his general health had remained good. He had had a dry hacking cough for years, which was sometimes precipitated by swallowing. The day of admission he passed a large quantity of blood by mouth; he could not say whether he coughed or vomited this blood. Associated with this episode he felt very faint and was immediately brought to hospital.

He did not smoke. There was no family history of tuberculosis and no significant environmental history. Except for an appendectomy, five years previously, and for the episodic bleeding noted above, he had always enjoyed good health.

He was well nourished but pale, and physical examination was totally non-contributory except that his pulse was 130 and his B.P. 86/40 mm. Hg.

The hæmoglobin value was 14.4 g. %, sedimentation rate 18 mm. in one hour (Westergren), and white blood count 16,300. Serology tests were negative, as were the urine analyses. A test for occult blood in the stool was positive. Sputum examinations revealed no pathogens or neoplastic cells. Serum proteins were normal, liver function studies were negative, the coagulogram was normal. Gastric analyses showed a trace of blood, with a slight elevation of the total and free acid.

The roentgenogram of the chest was normal. An œsophagogram (Fig. 1) disclosed a solitary diverticulum on the anterior aspect of the middle of the œsophagus, 5 cm. below the carina. The diverticulum measured about 2.2 cm. in its greatest diameter. The outline of the diverticulum was regular, except for the

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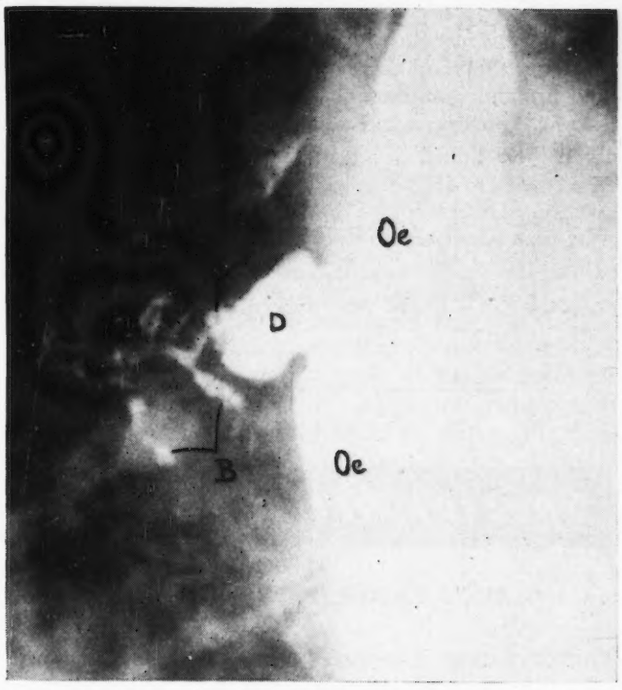

Fig. 1.—Roentgenographic examination of the œsophagus with barium showing the œsophagus (Oe), the diverticulum (D), fistula (F), and bronchus (B).

junction of a short fistulous tract ending in the right main bronchus. The barium after entering the diverticulum passed slowly into the bronchial tree. The lumen of the œsophagus appeared otherwise normal, as did the upper gastro-intestinal tract. A bronchogram showed no abnormalities except for a slight irregularity in the outline of the right main bronchus corresponding to the bronchial end of the fistula; the opaque medium did not penetrate into the fistulous tract. Endoscopy of the bronchi and œsophagus was negative; the diverticulum or fistulous opening could not be identified.

After admission, he was given 500 c.c. of blood and recovered from his mild shock. There was no further bleeding while in hospital. The patient for personal reasons left hospital and returned five weeks later, at which time a thoracotomy was performed. This was carried out through the bed of the 6th rib on the right side. The lung was retracted anteriorly after severing numerous thin adhesions posterolaterally. The mediastinal pleura was incised and the posterior mediastinum entered. By sharp and blunt dissection, the œsophagus was completely isolated below the level of the bifurcation of the trachea for about three inches (7.5 cm.). An œsophageal diverticulum measuring about 1.5 cm. in transverse diameter was found; this was directed upwards to the right main bronchus. Dissection of the diverticulum was easy, and led to a fistulous tract which bifurcated after a short distance. One arm of the Y communicated with the bronchus; the lower one petered out in the posterior mediastinum. The fistulous tract was isolated with the diverticulum and doubly ligated by transfixion and free silk sutures on the bronchial side. The œsophageal end was similarly treated, and both diverticulum and fistula were excised. The muscle fibres of the œsophagus were approximated with medium black silk interrupted sutures, and the mediastinal pleura was repaired. The pleural space was drained through the 7th intercostal space, by means of a 14 F catheter, and the chest was closed in routine fashion. A Levine tube was placed down through the œsophagus into the stomach. The postoperative course was uneventful. He was able to swallow liquids on the third day. He has been symptom-free for one year and there has been no further bleeding.

Histological examination of the resected œsophageal diverticulum showed it to contain a mucosa, lamina propria, muscle coats and serosa. The mucosa consisted of stratified squamous epithelium; no respiratory type of epithelium was seen. The lamina propria showed some œdema and there were scattered foci of chronic inflammation just deep to the squamous epithelium; in those foci there were dilated prominent capillaries. No areas of active ulceration were identified. Histologically the findings were those of a true œsophageal diverticulum with foci of chronic inflammation.

DISCUSSION

In the cases reviewed,[1, 2] trauma to the œsophagus resulted from gunshot wound or the swallowing of lye or foreign bodies. The trauma resulted in ulceration of the œsophagus; if penetration occurred, a fistula into the trachea or the left main bronchus was the outcome because of their proximity to the œsophagus. In the infectious type, syphilis, tuberculosis and non-specific organisms were found to be the causative factors. Coleman and Bunch reported a case where a tuberculous ulcer of the œsophagus perforated into the trachea without evidence of a pulmonary lesion. These authors point out that an œsophageal traction diverticulum may result from retraction of healed or healing tuberculous mediastinal lymph nodes or from adhesions secondary to Pott's disease of the vertebral column, or tuberculous or suppurative foci in the lung; tuberculous empyema, pericarditis, and syphilitic aneurysm of the aorta have also been listed as causative factors. Coleman and Bunch suggest that the fistula formation is always secondary to infection in the diverticulum with subsequent ulceration and perforation into the tracheobronchial tree.

The characteristic symptom of œsophagobronchial fistula is a sudden strangling sensation following immediately on the ingestion of food or fluid. This in turn is usually followed by paroxysmal coughing during which the ingested material may be coughed up from the tracheobronchial tree. It has been suggested[1] that this series of events will occur if the fistula is directed downwards from the œsophagus. Hæmorrhage has also been reported as a frequent and severe symptom. Maier[4] postulated that the bleeding originates from secondary pulmonary abscesses of the medial basal segments; these segments blend with the mediastinum, making the foci unnoticeable on radiological examination.

The case here presented is of interest from a diagnostic point of view. There had been no real symptoms associated with or precipitated by swallowing, except an occasional mild cough. This could probably be explained by the fact that the fistulous tract was directed upwards from the œsophagus.

The massive bleeding *per os* which necessitated admission to hospital was sufficiently severe to produce syncope and require transfusion. Although the patient's impression was that the bleeding followed a period of paroxysmal coughing, he could not be certain whether he had vomited or coughed up the blood. The melæna could have resulted from direct bleeding into the œsophagus or from the swallowing of coughed-up blood. The site of the bleeding could not be identified in the excised specimen; there was a five-week period between his last hæmorrhage and the operation, and a small mucosal ulcer could easily have healed in this length of time. The excised diverticulum did show marked chronic inflammation with congested mucosal vessels. The fact that the patient has not bled in the year following the operation makes it appear logical that the bleeding had occurred from erosions in either the diverticulum or the fistulous tract. The normal bronchographic studies rule out secondary pulmonary abscesses as a source of the bleeding. On histological examination, the excised diverticulum was found to be a true one, containing all coats of the œsophageal wall. Considering the age of the patient, the structure of the diverticulum and the areas of the œsophagus involved, one would have to conclude that this is an acquired diverticulum. In spite of the fact that at operation no factor such as adhesions or lymph nodes was found to explain the pathogenesis, it seems most likely that this was a traction type of acquired diverticulum. No past history of trauma could be elicited; the patient had had a Levine tube in his œsophagus after his appendectomy five years previously, but trauma to the œsophagus should not have resulted in this type of true diverticulum.

Various methods have been suggested in the management of œsophagobronchial fistula. Conservative treatment including endoscopic cauterization of both ends of the fistula has been advocated by Clerf,[1] along with temporary gastrostomy to exclude the fistulous tract from ingested food, and thereby promote healing. Surgical methods include excision of the fistulous tract with primary repair of the œsophageal wall and closure of the communicating bronchus; if inflammatory foci in the lung parenchyma are demonstrated, simultaneous segmental pulmonary resection is advocated. It appears that the operation is more rational, because conservative management includes the inconvenience of a gastrostomy, and cases have been reported in which the fistulous tracts have reopened after cauterization. Radical excision of the fistulous tract should offer permanent cure, and with present-day technique the mortality rate should be very low.

SUMMARY

A case is presented of a traction diverticulum of the mid portion of the œsophagus with a fistulous communication to the bronchus intermedius. The diagnosis was made by roentgenographic examination of the œsophagus. The presenting symptom was massive bleeding *per os*. Resection of the diverticulum with the fistulous tract and primary closure of the œsophageal and bronchial communications was carried out. The diagnostic features and advantages of surgical resection are discussed.

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Special Article

LUNG CANCER AND SMOKING

THE NATIONAL CANCER INSTITUTE of Canada was asked to undertake an assessment of the data concerning lung cancer and smoking. The following report has been made by a sub-committee of the Institute's Advisory Committee on Records and Statistics and has been approved by the Board and membership of the National Cancer Institute.

STATISTICS RELATING TO THE PROBLEM

(a) *Lung Cancer*

A recent study of mortality from cancer of the lung in Canada[19] indicated that, over a 20-year period, the death rate for this site of the disease as calculated from death certificates has increased approximately six times in males and approximately two and one-half times in females. This represents an increase in the total population of approximately four and one-half times. At the beginning of this 20-year period there were two male deaths to each female death from cancer of the lung and at the end of this period there were five male deaths to each female death.

At the present time in Canada cancer is responsible for approximately 16% of all deaths.[7] In turn, 9.5% of cancer deaths are attributed to cancer of the lung. It follows that cancer of the lung accounts for about 1.5% of deaths from all causes. These proportions may be expressed in the following way:

1. One death in six is caused by cancer.
2. For every ten deaths from cancer in other sites, one death is caused by lung cancer.
3. Of every 66 deaths in Canada, one is caused by lung cancer.

Among men the greatest number of deaths from lung cancer occurs between 65 and 69 years of age. Among women the greatest number of deaths is between 70 and 74 years of age. As calculated from vital statistics for males in 1956, the reduction in the expectation of life due to lung cancer is approximately four months.[18]

The vital statistics of other countries such as Denmark,[4] Britain,[22] and the United States[9] show an increase in lung cancer deaths as great as or

greater than in Canada over a corresponding period.

(b) *Smoking Habits of Canadians*

For the year 1935 the average number of cigarettes smoked per person in Canada was approximately 490.[8] In 1955 this figure was approximately 1500. This represents a threefold increase.

In 1956-57 approximately 65% of Canadian men, 18 years and over, smoked cigarettes as compared with 35% of women.[25] Among 100 cigarette smokers 51 of them smoke 10 cigarettes or less per day, 39 of them smoke approximately 20 cigarettes per day and 9 of them smoke more than 20 cigarettes per day. The smoking habit is less prevalent among country dwellers and the average daily consumption of cigarettes for this group is less than for city dwellers. In 1956 the Canadian Government sold excise revenue stamps to cover the sale of 26,997,705,000 cigarettes.

LUNG CANCER IN RELATION TO OCCUPATION AND ENVIRONMENT

There are a number of reports in the medical literature which suggest a relationship between lung cancer, occupation and environment. For several hundreds of years a high percentage of miners in Schneeburg and Joachimsthal in Eastern Germany and Czechoslovakia[15] have succumbed to chest disease recognized only in this century as cancer of the lung. Although complete evidence is lacking as to the cause, radioactive gases may be responsible.

On several occasions recently the Chief Inspector of Factories in England has mentioned the appearance of cancer of the lungs in workers exposed to the inhalation of the dust fumes of arsenic.[1]

Since 1932 a high incidence of cancer of the lung has been noted among workers in the chromate industry. A recent study[16] of several chromate industries in the United States showed that lung cancer occurred almost 20 times as frequently among male employees as among the general male population. In 1932 it was also reported from South Wales[2] that there was a high incidence of cancer of the nasal sinuses and lungs in men who refined nickel ore. A less well defined relationship is that between cancer of the lung and asbestos disease of the lung.

Japanese doctors in 1936[14] reported a high incidence of lung cancer among stokers exposed to the inhalation of hot tar fumes in a Japanese gas generator plant. It has also been observed that deaths from cancer of the lung are more frequent in urban than in rural areas, suggesting that smoke, industrial wastes, fumes from motor vehicles or other factors peculiar to city life may be related to lung cancer.

CIGARETTE SMOKING AND LUNG CANCER

In reviewing the literature on the relationship between cigarette smoking and lung cancer it seems important initially to point out that all cases of cancer of the lung cannot be accounted for on the basis of cigarette smoking, because the occurrence of lung cancer in persons who have never smoked is not at all infrequent. Medical literature, however, contains the reports of at least 16 studies carried out over the past 18 years in several countries and in each of these a statistical association has been noted between lung cancer and smoking.[6, 23, 27] These studies have been of two types, retrospective and prospective. Retrospective studies are based on an analysis of the smoking habits of patients with lung cancer. Prospective studies have determined the incidence of lung cancer in special groups over a period of years among persons who smoke compared with persons who do not smoke. In summary these studies show that lung cancer occurs 5 to 15 times more frequently among cigarette smokers than among non-smokers. The incidence of lung cancer increases with the amount smoked, and the cessation of smoking by heavy smokers is accompanied by a lower risk of such individuals developing lung cancer. Another type of study has shown that the air passages of the lungs of smokers more frequently show microscopic changes generally associated with malignant transformation than do the air passages of non-smokers.[3]

The main criticism of these studies has been of bias in sampling or, in other words, that the groups chosen for analysis had not been representative samples of the general population. In our opinion such factors are not of sufficient weight to destroy the validity of the conclusions drawn from the studies. Again, it has been suggested that the demonstrated association between lung cancer and smoking may not be one of direct relationship, but rather one related to a third factor. In other words, whatever constitutional factors may be playing a part in making a person a smoker may, singly or collectively, be the factors responsible for the tendency to develop lung cancer, rather than cigarette smoking itself. The possibility of this being so cannot be denied. We think it important to point out, however, that scientific proof free of criticism, of a cause-and-effect relationship between lung cancer and cigarette smoking can only be obtained by experiments of an impractical kind. It would be necessary, for example, to take thousands of pairs of ten-year-old children and, for each pair, toss a coin to determine which member of the pair would be asked to take up smoking and which would not. By this procedure smokers and non-smokers would be chosen without reference to any other trait in their nature so the bias of any third possible constitutional factor would be removed. These individuals would then be followed up for the remainder of their life, and appropriate studies made of the numbers who died of lung cancer and other diseases.

In addition to these studies on humans there are reports[10, 20, 21, 24, 26] concerning the production of malignant tumours in animals by the condensates of tobacco smoke. However, there are also reports[5, 11-13, 17] of similar tests in which negative results were obtained, that is, in which no malignant growths were observed. Conclusions drawn from animal experimentation do not, of course, necessarily apply to humans.

From the practical standpoint, further findings of a possible cause-and-effect relationship between lung cancer and cigarette smoking can be expected to come only from: (a) continuing epidemiological studies of the kind already reported and (b) further

studies relating to the detection, isolation and biological assay of substances in tobacco smoke that may be suspect.

In our opinion the most important fact arising from this review is the following: While it has not been established that cigarette smoking is a cause of lung cancer, statistical studies show that cigarette smokers have a greater risk of dying of lung cancer than have non-smokers and the risk increases with the amount smoked.

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REVIEW ARTICLE

OBESITY

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OBESITY is statistically defined in terms of excess of ideal body weight. The threshold of percentage excess given[1-3] varies from 10 to 30%. Hence calculations of the prevalence of obesity in the population also vary widely. Thus it has been stated that more than 20% of North Americans are too fat.[4] "Ideal" body weights are given in tables issued by insurance companies.[5] These tables of current normative figures are dependent on sex, age and height. Actually, there is nothing "ideal" about these weights because:

(a) They cannot be adjusted to the body build of the person which may account for at least ± 5% of normal variation for the type, i.e. pyknic, leptosome, endomorph, etc.

(b) They are not weighted for ethnic, socio-economic and ecologic variables. The ideal for an English parish priest may not be the same as that for an Italian bishop. And most importantly,

(c) they are not compiled on the basis of what the weight *should* be to avoid the morbidities and the mortality attributable to obesity. In any case, body weight is not necessarily a parameter of body fat. In a study of overweight, robust footballers, it was established[6] that their bodies contained less than the normal 10% fat, the excess being due to muscle and bone. The opposite is also true, namely that it is possible to weigh within normative limits and be obese because of the presence of more than 20% of fat content in body weight, as measured by specific gravity or radiological techniques, or post-mortem chemical methods. Thus obesity is best defined as accumulation of excessive adipose tissue. The diagnosis is made on each individual. Inspection and palpation of the body, the use of calibrated skinfold calipers and consideration of sex, age, height, body build, preferred weight, history of weight cycles and fluctuations, occupation, habits and sense of wellbeing are essential for accuracy. Studies on obesity lacking this descriptive definition of their subjects fail to convince. Descriptions may also gain from a classification of fat distribution like: android, gynoid, sponge-like, or endocrine.

It has been calculated[6] that North Americans contain 125 million tons of extra fat whose energy would yield 100 billion calories of heat. More seriously, it has also been calculated[7] that for each lb. of overweight in the 45-55 age group, the mortality increases by 1%; that the overall mortality from 20-64 in the obese is 50% higher than in the normals and that the association between obesity and nephritis, diabetes or cirrhosis increases the mortality of the disease from 90-150%.[8] Being traditionally statistically conscious, no wonder America has become weight-conscious. This may be a bad thing by itself, for self-consciousness leads to anxiety, anxiety often leads to overeating, and overeating is the main mechanism of obesity. Thus public education must be prudent.

The list of penalties incurred by the obese is terrifying. It varies from diseases in which excess fat is pathogenic, to those in which it complicates the clinical picture—to the extent of added morbidity and earlier death. This list includes manic-depressive psychosis; hypertension, atherosclerosis, coronary thrombosis and generally cardiovascular disease, venous thrombosis, varicose veins, embolism; diabetes, cirrhosis; nephritis; gall-bladder disease, appendicitis; degenerative arthropathies; increased incidence and complications of fractures; higher fetal mortality, complicated delivery and

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toxæmia; increased surgical risk during anæsthetics and owing to delayed wound healing; increased incidence of hernia and secondary polycythæmia due to emphysema and a high diaphragm, hence embarrassment of pulmonary ventilation, and finally anoxia. Cancer and suicide are doubtfully associated with obesity. Small consolation that pulmonary tuberculosis and peptic ulcer are significantly unassociated with obesity. All this suggests that obesity is the most important problem of public health in the West.

Faithfully did King Henry counsel Falstaff: "Make less thy body hence, and more thy grace; leave gormandizing; know the grave doth gape for thee thrice wider than for other men." Unfortunately, psychiatrists have found, as did King Henry, that this kind of wisdom is lost on the outwardly sensuous devotee of Epicurus and Bacchus who is inwardly driving death. As one of them, who shall remain anonymous, cynically replied on behalf of Falstaff, "Since life consists of filling a gap between one stinking hole and another, I mean to fill it well and truly!" Obesity follows the second law of thermodynamics. Lavoisier, Laplace, Liebig, Voit and others have long attempted to apply the law of conservation of energy to living organisms. The French clinicians of the 18th century had the modern working hypothesis that excess fat will result from excess intake over output.[9] This has been reaffirmed with unnecessary zeal in the 20th century. The following single formula is due to Newburgh,[10, 11] a painstaking pioneer in this field, "Obesity is due to an overall intake of energy which has exceeded the total dissipation of energy of the body, i.e. a positive energy balance". Clearly, if 30 million North Americans are too fat, this cannot be due directly to endogenous, hereditary, neuroendocrine, or inborn metabolic errors per se. Neither nature nor unnatural selection could be so ungenerous. Newburgh exculpated two of the usually claimed causes: (1) "The body is inherited, obesity is not." This is supported by Rynearson,[12] among others, who doubts the constitutional basis of obesity. (2) "Obesity is never directly produced by increase or decrease of endocrine activity." Hormones probably control the distribution and long-term storage of fat—hence the buffalo fat, full-moon face and inverted olive-on-a-toothpick body of Cushing's syndrome. Newburgh and others have proved that in the obese there is no specific disturbance in intermediary fat metabolism, no hypometabolism, no faulty water retention (except perhaps in some premenstrually obese women), no disturbance in fat digestion, absorption, assimilation, no disturbance of carbohydrate enzyme mechanism or in glucose release and utilization, no change in the specific dynamic reactions of proteins and food in general, no disturbance in the capacity to mobilize fats, and probably no special lipophilia of adipose cells and likely no pathology in the mechanism of weight reduction. Yet the following disorders are commonly associated with overweight or more likely with obesity or with abnormality of fat deposition: hypothyroidism, castration, the menopause, diabetes, Cushing's syndrome, Fröhlich's syndrome and especially macrosomia adiposa congenita, fronto-hypothalamic-midbrain pathway lesions due to cysts, tumours, encephalitis, injury, fractures of the base of the skull, frontal lobotomy, idiocy and generally mental deficiency, Dercum's disease, Klein-Devine syndrome which is a frontal-lobe bulimia, and finally the lipoidoses, not forgetting the sex-linked steatopygia of Australian Bushmen and Hottentot women and also the Laurence-Moon-Biedl syndrome with or without the Morgagni-Stewart-Morel associated syndrome. But all these taken together may account for from 2-3% of obesity.[12] The inescapable conclusion is that too many people are too fat because they eat too much and probably because they exercise too little. Interestingly enough, even men and experimental animals with neuroendocrine lesions get fat only because they overeat and not directly because of their lesions. Eating is carried out at the painful instigation of easily satisfied hunger, while overeating is indulged at the pleasurable behest of appetite. The whole physiological regulatory system is normally so robustly poised that, despite excesses of eating and of burning up energy over the years of life, a normal balance exists which precludes thinness and fatness in most people, most of the time. Clearly, the pathogenesis of obesity in the individual depends on the physiology of hunger, the psychology of appetite, the psycho-physiology of activity and of weight adjustment-reduction; against the general matrix of ethnic, genetic and constitutional endowment, the socio-economic-ecologic background for the availability of food, the cultural customs and values regarding eating and corpulence; and against the particular matrix of individual inheritance and constitution resulting in body build and of the family interpersonal dynamics and personal customs and values. Obesity has been called a self-limiting neurosis. It is, in fact, the pristine psychosomatic problem. The difficulty in elucidating such necessarily complex human problems is the confusion created by specialist workers in different fields emphasizing the value of their particular concern often to the exclusion of other considerations and thus preventing an integral view. The problem of obesity is bedevilled with prejudices arising from ignorance, such as that hypometabolism is equivalent to hypothyroidism and that this is responsible for obesity; or that diet as such accounts for overweight or that the output aspect of physical activity is unimportant in the equation that leads to excessive intake, hence accumulation of adiposity. The problem of obesity is further confused by researchers who do not separate the primary pathogenic factors of, say, economics and the symbolic value of food for the obese or the perversion of oral drives, from the physical mechanism or physiologic pathway

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through which the primarily pathogenic factors find somatic expression. This led to the idea of a multiple physical causation. Instead, it would be more justifiable to think of the many short-term and long-term ways in which the physical mechanism may be disturbed by a primary psychosocial constellation of factors pertinent in each individual. Thus it may be that the physical pathway of obesity may be accounted for through Bruch's[13] theory of the dynamism of fat storage controlled by the autonomic nervous system, or perhaps by the neuroendocrine control of lipophilia in adipose cells. Bauer[14] had a similar theory of a change in local fat storing ability. This may be a long-term mechanism. On the other hand, the most promising hypothesis for short-term mechanisms of satiety may be the glucostatic theory of Mayer,[3] supported by Portis[15a] and recently expounded by Stunkard and Wolff.[15b]

The story of the mechanism of obesity is a story of mice and men. It was found in follow-up experiments of the Houssay preparations that lesions and stimulations of the ventromedial and ventrolateral nuclei of the hypothalamus produce hyperphagia or anorexia and thus that these centres act as feeding or satiety stations. These centres are on the cortical, thalamic, rostral and tegmental mesencephalic system and thus linked to the frontal cortex and the visceral-rhinencephalic brain. Small lesions produce voraciousness analogous to the night-feeding syndrome of the obese or the secretive gorging of some patients with anorexia nervosa. Large lesions lead to persistent hyperphagia and active obesity. In man, lesions affecting the feeding centres may lead to overeating and so-called cerebral bulimia. Also it is known that functional hyperinsulinism, insulin subcoma treatment and uncontrolled diabetes result in hyperphagia. The brain is entirely dependent on blood glucose for its respiration and nourishment. Hence it is postulated that the hypothalamic satiety centres are glucoreceptive, alerting the brain and hence the person to a fall in available blood glucose, as measured by arteriovenous differences and by direct measurement of the level of glycæmia. Some suggested that hunger contractions in the stomach and activation of sensory oral organs of appetite, including salivation, may be associated with hypoglycæmia. This has not been shown consistently. In their researches Stunkard and Wolff set out perhaps too laboriously though not statistically to show: (1) that hunger contractions were not regularly associated with hypoglycæmia; (2) that there was no disturbance in the "glucostatic" mechanism of the obese. This proof might have been thought unnecessary because, as we mentioned, it seems highly unlikely that 30 million North Americans have an inherent fault in metabolic mechanisms; moreover, there is no evidence that functional hyperinsulinism which does lead to hyperphagia also results in active obesity; nor does the "cerebral bulimia" of animals or man necessarily result in obesity. Stunkard and Wolff suggest that: (1) there may be a relationship between glucose utilization and hunger; (2) there may be a disturbance of glucose utilization in the obese. Newburgh's work tends to refute both this hypothesis and that of a disturbance in gluconeogenesis. Stunkard and Wolff then put forth rather an ingenious theory: that irregular feedback signals from such patterns as the night-eating syndrome of some obese upset the glucostatic regulation of satiety. They attempted to link up their postulated mechanism with instinct theory from the point of view of source of oral drives. They suggest that a specific symbolic factor, namely threatened loss of emotional support of a particularly significant person and associated with depression, throws the oscillating system of satiety out of gear. Such psychodynamic specificity is denied by other workers[6] and by the generally disappointed searchers into psychopathologic specificity in psychosomatic syndromes. At the inception of their work the authors failed to distinguish clearly between hunger and appetite. They worked in the acute experimental situation of hunger, rather than on disturbed appetite. Later they recouped somewhat by the ingenious introduction of hypnosis to show that hunger contractions can be suggested without a chemical stimulus, i.e. by symbolic process, and thus they smudged somewhat the hitherto clear line of distinction between the physiological mechanism of hunger and the psychological one of appetite. Lastly they showed that with increased peripheral utilization of glucose —presumably when the glucoreceptors in the hypothalmic feeding centres are satisfied—there was no hunger contraction, even under hypnotic suggestion. Altogether, this work, though somewhat confusing and contradicting previously known facts, may, if doggedly pursued, open the way to an integral psychophysical mechanism theory.

It is entirely possible that the psychophysical mechanism for sudden obesity following trauma or psychic shock differs from that subserving gradual obesity. It is remotely possible that, as Mayer puts it, there is multiple causation—that is, several possible pathways manifesting the disturbance. But it is more than likely that an integral psycho-neuro-endocrine mechanism exists, and researchers have the onerous task of finding the missing links.

The etiology of obesity abounds with hunches but hardly any controlled study to establish the facts. For instance, there are obvious ethnic differences between the underdeveloped and western countries making for different weight norms. There are cultural food value differences between say, on the one hand the Pennsylvania Dutch, the Italians, the European Victorian woman especially from the mid and eastern part of the Continent, and the Hebrews, all of whom tend to equate food with parental affection and size with health and strength, and on the other hand, Anglo-Saxons, Scandinavians and especially the Highland Scots,

who consider frugality a virtue. Food is part of religious symbolism and of rituals involving fasts and feasts, and sacrifices. There are social values in the fellowship of breaking bread, in parties, fiestas and fraternity dinners. There are culinary taboos round the world forbidding every kind of dairy product and meat except mutton. Then there are ecologic[16] differences between the plainsman and the agriculturist; the fur trapper and the banker; the American switchman and the railroad clerk; the Italian steelworker and fireman; the Swedish shipyard worker and clerk and the Japanese farmer and physician. There are occupational hazards for obesity, or perhaps choice selections by restaurateurs, brewers, confectioners and even those men of business who conduct it best round a well-laid table. Modern environment provides shorter working hours and increased passivity in leisure hours in attendance at spectator sports, film and television viewing, radio listening and perhaps above all in the availability of means of transport, like the motor car in which the driver expends just 0.9 calories per kg. wt. per hour. Increased passivity in locomotion in accumulated time may be represented by the following calculation. All else being equal, if a man meeting his energy costs walked briskly, swam, skated or bicycled regularly for one hour instead of sitting and drinking a martini and eating 10 cheese crackers or drinking two bottles of soft drinks for the same hour daily, he would accumulate in the order of 30 lb. of (fat) weight a year; or if a woman also otherwise meeting her energy costs sat and drank three extra cups of coffee with sugar and cream instead of walking briskly or playing volley ball for the same time daily, the difference would be of the order of 40 lb. a year. In an obese person, that is 20% heavier, the cost of exercise rises in proportion to the power needed to move the body weight; thus the difference in expenditure of energy between an active obese person and a passive non-obese one is larger by a fifth.

We lack sufficient longitudinal studies of the natural history of obesity. It may occur developmentally from childhood or appear later, characteristically at periods of psychoendocrine changes such as adolescence, after marriage, after a child, menopausally, after prolonged immobilization or in convalescence following an operation, an illness or a sudden shock. We know that there are in the course of life of many people, phases of hyperphagia, then active weight gain, followed by anorexia and weight loss or else by a quiescent plateau from which the weight ascends. These swings may be rapid in some and then they are often associated with periodic anxiety or depression and elation, or they may be wider spread over the whole life. Yet others eating well maintain a steady weight throughout life. There is an analogous situation in some women who retain more Na, Cl, water and weight than others premenstrually. They may or may not lose all their extra weight postmenstrually. Yet others do not retain any water and electrolytes and maintain a balance throughout. We know that there are people who eat when they are anxious and perhaps as many who have anorexia under or after a strain. Only some of those who eat for sedation of anxiety become obese. There is evidence that the pattern of eating is more important than the diet or even perhaps a variation in calories. The fast, voracious night feeder, eating all his calories at one sitting and often being anorexic in the morning, is more predisposed to obesity than the steady slow eater. In terms of diurnal variations of eating habits it would be interesting to learn whether Asiatics (such as Hindus or Persians) who can afford to eat bulk and calories, and whose habit it is to eat a large meal at sundown, burp politely and if old-fashioned regurgitate and eat some more, get fatter than shall we say Europeans like Bavarians who eat the equivalent calories in divided doses. Margolin[17] looking at the obese was impressed by their addiction to food comparable to other addictions. But then would he find a significant relation to obesity if he began by looking at those addicted to food? This is the same argument as that applied by those fond of explaining disorders on the genetic basis. Looking at the obese one finds a large incidence of obesity in their parents[18] (87%) and in their identical twins, while that of fraternal twins is no higher than in siblings. But looking at the children of obese persons one finds a surprisingly low incidence of obesity among them. Clearly we do not know the operative factors of natural history. Turning now to psychopathology, control studies are sadly lacking. What is more lamentable is that there are no imaginative qualitative analytical parallel studies of patients with similar psychopathology presenting with equivalent yet contrasting syndromes such as anorexia nervosa, peptic ulceration and neuroses without obesity; and, vice versa, patients selected for the same presenting syndromes with contrasting psychopathology. It is established that there is no specific personality prone to obesity. Nor is the fat person jolly and good-tempered, though some who hide quite a contrary nature may appear so because of their need to be accepted and liked.

Shorvon[19] stressed the family relationships. Typically mother runs after roly-poly Johnny with the pudding and the plea "Eat it for me—please!" Mealtime is the all-important locus of family daily reunion when conditioning to the cross-currents of emotional climate intermingles with the customs of eating. These connections then become established, learned. Bruch,[20] who dedicated a lifetime to the study of obesity in childhood, emphasized the dominant role of the mother who is incapable of giving her child love and may even unconsciously reject him; she substitutes food for tenderness. In her purchasing "the food of love" she spends a disproportionate amount of father's money, thus making him pay through his nose for the child he

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gave her. She judges good health and strength by roundness and fatness. Mostly she did not want a child, and the youngest or only child bore the brunt of her feeding affection. The consequences are that the youth is rejected by the group as spoilt, unsporting, stout, shy and awkward. This leads to self-repugnance and hence to ambivalence in psychogender which is felt most acutely in adolescence. Thence anorexia may begin or obesity proceed, or, if the situation is rectifiable, there may be a resolution. If there is no resolution, heterosexual adjustment is poor and self-perception becomes so distorted that unless the person feels bulky and is reflected by society as having considerable substance he develops a feeling of nothingness, of not being. Between adolescence and middle age the obese psyche may be caught in such a maelstrom that it seeks refuge in the psychosis of the beauty salon.

In spite of Bruch's brilliant and devoted study, because of the lack of controls there is no proof that any one family constellation of interpersonal dynamics and values will result in obesity.

The psychogenic precipitants which may result in obesity are often sudden and deprivatory such as bereavement through loss of a loved parent, spouse, or a fortune, an established job, through social or economic failure or a threat to the body.

The search for specific symbolic distortions accounting for overeating has yielded a maze of factors: hyperphagia to assuage and sedate anxiety and indecision; substitution of oral pleasure for failure; dispelling boredom; seeking praise and acceptance; compensating for deprivation; repressed hostility reactivating primitive cannibalizing impulses aimed at eating the enemy who is substituted for by food, and the reverse feeling with the same result: of yearning for a lost person or situation, such as wished-for happy childhood, and orally incorporating the lost person or returning to the primitive oral state of mind: self-reward (amusingly enough this is often given for being good about sticking to a diet for a while); defiance of authority yet exercising restraint and submission in other respects—in children this and deprivation is often connected with stealing candies directly or money to buy candies and frequently to buy friends; hoarding is a related form of behaviour. In younger children there is the related condition of pica and coprophilia; midnight gorging is also a related form of behaviour; eating oneself into the grave may be associated with desire for self-punishment and self-degradation to expiate guilt and to justify rejection by others. Self-punishment or the fear of losing one's body strength may be reacted to by the desire to conserve the self, with an incidental positive energy balance. This may be manifested in the psychotic by the impulse to eat fæces and drink urine and semen. Fatness may represent an exhibition of corpulence for attention, to test a doubted affection on the part of a mate or parent; as an identification with a fat parental figure; to avoid competitiveness in sexuality; as an overcompensation for the traumatic experience of actual starvation in earlier life during periods of poverty and deprivation. In the context of sexuality, obesity may be offensive or defensive, a bid for acceptance or a wish to be repulsive and thus left alone and out of the running. A girl's overeating may result from penis envy expressed also with the phantasy of incorporating the male phallus. In childhood the sex theory of oral impregnation is prevalent. To the child's mind, rather logically if the baby is in the tummy, it gets there through the mother's eating too much. Later the child associates oral impregnation with the illicit kiss. Overeating may be a symptom of sublimated drives or the result of unsublimated oral drive. Semasiologic analysis would probably bring out the apparent symbolic heterogenity resulting in eating and reactive to it. A sample of such phrases: "can't stomach him", "could eat her", "like a peach", "honey", "sour face", "makes me sick", gives the general idea. The usually oversimplified Freudian doctrine in this instance "explaining" obesity in terms of orality is overrun by the gamut of psychopathologies found to be associated with it. Bergler[21] arranged the various psychogenic factors of obesity in terms of theories, viz. (1) the bad mother relation, offering food; (2) substitution theory, food for love; (3) the combination theory when the child is making up to the mother's frustrations in over-gratifying her feeding impulse; (4) the statistic misunderstanding of libido with increased oral eroticism to make up for lack of healthy gratification; (5) the separation theory of bereavement; (6) association of starvation in the past, to which should be added (7) Bergler's own theory of statistic misunderstanding of libido resulting in psychic masochism. Yet at this level of causality as in consideration of psychophysical pathways there is probably some hierarchical order. Moreover in the stratified levels of the symbolic process in the individual, the principle of over-determination by a group of significant factors probably governs. That is, at different levels of integration significant factors operate in the individual, probably with some specific selectivity, eventually summated past the threshold that maintains the regular balance of weight. Despite Kaplan,[6] in the overall picture food is a substitute for love and security, and regressive oral pleasure is transmuted for the gratification of insatiable neurotic appetites in the context of deprivation and its various reactivations. All this may lead to a pathological increase in appetite and then perhaps to a psychophysiologic shift in the hunger-satiety mechanism and intake; obesity results. The person then eats to get fat, for the amazing regulatory mechanism which keeps weight constant has to be overcome to allow the body to accumulate energy.

Looking now to the other side of the energy equation, namely the output of energy, it has been found that the obese are increasingly in-

active. Bruch showed that 72% of 140 obese children were physically inactive but their inactivity did not correlate with the severity of obesity. It is well that Stunkard,[22] the author whose papers we have already discussed, ignored such misleading statistics as: To lose a pound of fat a person has to walk for 36 hours, split wood for 7 hours or play volley ball for 11 hours. He also circumvented such fallacious opinions as: any loss of weight would be compensated by hyperphagia to make up for it. Amusingly enough, if the obese mice bred with the recessive hyperglycæmic gene are crossed with the waltzing gene they increase their level of activity by several hundred per cent, with the result that their weight increase is only some 20% that of normal mice whereas the non-waltzing hyperglycæmic obese mice are some 200-300% fatter than the normals. However, one must add that no one has to our knowledge measured the energy differences in output between the recessively obese Shetland shepherd dog and the greyhound or between the fat bred hogs and the others. Nor have Stunkard and Wolff, using the pedometer as a device and finding that obese women walk 2½ times less than the non-obese, proved that they actually expend less energy. It is known that the obese expend energy in proportion to their weight; consequently the exercise costs them more than the normals. The question remains—do they have periods of relative immobility and voracious ingestion in which they permanently raise their weight plateau? And do they then remain sufficiently less active to maintain and later increase their weight?

Finally, in considering the treatment of obesity all authorities agree that drugs and hormones complicate the issue and cause failure. A simple and direct approach to dieting, strict or indulgent, without considering the psychosocial factors, the current mental state and psychology is not only fruitless in the long run but may be actually deleterious in the short run, for it may precipitate dieting depression,[23] psychosis and even suicide. At no time should an ambulatory patient receive less than 1000 calories a day. Kekwick and his associates at the Middlesex Hospital found that a "ketogenic" diet of 90% fat is better tolerated by the obese for as long as two weeks than by the non-obese. It has the advantage of interfering drastically with the mechanism of hunger but the disadvantage of leaving out therapy of primary pathogenesis.

Some experts have left the diet to self-selection while concentrating on the education of the patient, stimulating his positive motivation by tickling his pride in physical appearance, by alerting him to the danger of illness, and by protecting him from the pressures of relatives and well-meaning friends. They found that encouraging the patient to keep a diary of diet and events with no more than a weekly entry of weight gave him a chance of gradual insight and self-regulation of intake and activity. It was found expedient to treat obese children by involving their parents in psychotherapy, with the resultant loss of weight in the child. One of the most successful approaches has been made through group psychotherapy. Kotkov[24] reported that 26 patients lost an average of 10 lb. and maintained this for one year at follow-up. After 10 sessions 48% maintained their weight loss as never before.

It struck us that one of the keys to weight reduction is that many obese deny their problem, often omit it in recounting their symptoms, and report falsely on their food intake. This reporting is so mendacious that Mayer[3] actually fed his patients, under controlled conditions, the calories they said they ate and the obese lost weight on it. This false reporting is likely part of a mental mechanism of denial, in keeping with the archaic pattern of the defence of the obese and analogous to agnosia. This denial is associated with a distortion of body imagery, thus providing a faulty link between somatic reality and the motivations assaulting the symbolic processes. Probably this denial of the image of the actual body extends from unawareness of quantity and frequency of food ingested to denial of corpulence reflected in a plane mirror. We wondered whether the treatment of obesity would be more effective if the free-choice diet, the self-directed insight derived from diary keeping, and individual and group psychotherapy were combined with a periodic projection of a stereoscopic (3D) colour film of the patient's body in all perspectives and appropriate disrobements.

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THE STRENGTH OF WORLD MEDICINE

At its Twelfth General Assembly and the Council sessions which preceded and followed the Assembly in Copenhagen in the latter half of August, the World Medical Association covered a wide range of topics of interest to every physician. Two of these topics which are of fundamental importance for the practice of medicine were discussed by speakers at the opening session. One is the right of organized medicine to be consulted on any matter concerned with the health of the people, and the other the divisive influences tending to weaken the voice of organized medicine and therefore to diminish its effectiveness in consultation with bodies outside the profession.

Now neither of these topics is new. Organized bodies of physicians have complained frequently in the past that they were not consulted about health measures by governments (sometimes because governments grew weary of the conflicting opinions they gave), and medical statesmen have lamented on many occasions in the past century the lack of unity within the profession.

But some things need saying again and again ad nauseam, just as persons have been reciting the Ten Commandments for centuries to remind themselves of disagreeable but necessary components of good behaviour. And so we are grateful to the new President of the World Medical Association, Dr. Charles Jacobsen of Denmark, when he reminds us once more in his inaugural address that "the most important task of every national medical association is to exercise a decisive influence upon the solution of the problems concerned with the health of the community, both general and individual". And we are delighted to hear a government spokesman, Dr. Johannes Frandsen, Director General of the National Health Services of Denmark (a country with a fairly highly developed social security system), state to the Assembly that "The medical profession has a fundamental right to be consulted when the lines for the future development of a health system are to be plotted —not so that they may be drawn reluctantly into a new era . . . . but to meet developments as they come, receive what is new and help to mould it with the aid of the old but ever-young ideals of the profession."

The profession must constantly remember that this right is not admitted by many planners and politicians in some parts of the world, and that our colleagues abroad have often suffered in recent years from this disregard of their advice. With this shrinking world, a threat to some must eventually mean a threat to all.

There is, of course, a price to be paid for the right to influence public and political opinion. It is the high price — difficult to meet in this age of specialties and subspecialties — of professional unity. Says Dr. Jacobsen, "A united medical association *including the entire medical profession* is essential in obtaining a decisive influence" upon the solution of community health problems. He added that for effective action globally the World Medical Association must apply the same principles necessary for successful action nationally. This means that W.M.A. must have the generous support of its national member associations if it is to act as a successful counterpoise to the government-controlled organizations which claim to determine the destiny of medicine.

Finally, we commend the quotation by Dr. Jacobsen from the founders of the Danish Medical Association:

"To stand united, to persevere and to show moderation, therein must an association such as that of the medical profession seek its strength, and therein lies the strength."

Editorial Comments

ENCEPHALOPATHY AND INFLUENZA

To feel "out of sorts" for several days after an attack of influenza is common, but severe neurological complications are rare. Of considerable interest therefore are recent reports of an encephalitis-like syndrome[1, 2] or psychosis[3, 4] which occurred during or a few days after attacks of influenza during the epidemic caused by the Asian type A influenza virus last autumn and winter.

Flewett and Hoult[1] present good evidence of recent infection with Asian type A influenza virus in three groups of patients with neurological disorders. Influenza virus was isolated post mortem from the lungs of five patients out of six who developed encephalitis at the height of the influenzal attack. The brains of these patients, although congested, showed no perivascular cuffing or other evidence of invasion by virus. A further four patients developed encephalitis three days to two weeks after onset of influenza. Elevated complement-fixing antibody titres to influenza A antigen were found

in convalescent sera from these patients, thus confirming the recent occurrence of influenza. Two patients, one of whom died subsequently, developed ascending paralysis seven and eleven days after onset of an illness which was shown serologically to be due to influenza A virus.

Grossly abnormal electroencephalograms[2] were found in three patients out of four who developed non-fatal encephalitis four or five days after an attack of influenza. High titre complement-fixing and haemagglutinin-inhibiting antibodies to the Asian type A virus in convalescent sera from each patient confirmed that they had recent infections with this virus.

Psychosis appeared as the only clinical manifestation of neurological abnormality two to ten days after attacks of influenza in three young patients in Jerusalem[3] and in 19 older patients in Barbados.[4] Electroencephalograms taken in all three Jerusalem patients were abnormal, and high titres of influenza A complement-fixing antibody in convalescent sera suggested recent infection with influenza virus. None of the Barbados cases was investigated virologically.

Although the possibility of pre-existent mental instability in two of the Jerusalem patients and several of the Barbados ones is strong, rendering them especially likely to break down under any stress, emotional or febrile, the time interval between the attack of influenza and the onset of psychosis was similar to that for encephalitis following influenza. This suggests that if neurological abnormalities become apparent following infection with influenza a wide spectrum of different syndromes may result, depending on the individual host's reaction to infection.

Although the NWS strain of influenza A virus[5] has been adapted to grow in the brains of mice after repeated intracerebral passage of the parent strain WS, and the non-neurotropic strain MEL has given rise to neurotropic progeny by recombination,[6] there is no evidence that field strains of influenza virus have invaded the blood stream of man and multiplied in the brain. The human disease influenza normally results from multiplication of influenza virus in the bronchiolar epithelium, with spreading of catarrhal inflammation throughout the bronchial tree.[7] The pathological picture in brains of those patients dying of encephalitis following influenza was not consistent with invasion by influenza virus. In only one instance was influenza virus recovered from the brain, and this probably was due to contamination with virus during removal of the brain.

Encephalitis may complicate infection by mumps virus in 0.5 to 10% of cases of parotitis.[8] Less commonly, encephalitis complicates the course of infection with chickenpox or measles virus. Despite the enormous number of cases of clinical influenza due to Asian type A virus, extremely few cases of interference with cerebral function have been encountered. Recent reports now strongly suggest that the usual attack of "flu" caused by the Asian type A virus may occasionally become complicated by an encephalopathy which is manifested clinically as encephalitis or psychosis.

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MEDICAL TREATMENT OF HYPERTENSION

It is only seven years since the chief of a nephritis and hypertension clinic opened a discussion on the medical management of hypertension with remarks which were pessimistic and even nihilistic regarding the value of drug therapy. He would not even concede any value to phenobarbital, except as an adjunct to psychotherapy. No amount of prodding by other participants in the conference could make him concede any effect to measures other than bed rest, alcohol and psychotherapy.[1] While this attitude was opposed by some of the participants, it is nevertheless significant that such an uncompromising stand was taken by a physician with extensive clinical and scientific experience in this field. The change in attitude towards treatment of hypertension in recent years is best epitomized in a symposium held recently at the Mayo Clinic.[2]

Fairbairn deals with the selection of hypertensive patients for drug treatment, and points out that most patients with "diastolic" hypertension ought to be treated. He describes briefly the steps to be taken to eliminate secondary hypertension, including such specialized procedures as aortography, and enumerates the causes of secondary hypertension. Certain situations call for emergency antihypertensive treatment. Such emergencies are encephalopathy, pregnancy in a hypertensive patient, and cerebral hæmorrhage. The contraindications to such treatment are a severe degree of renal insufficiency, severe psychiatric disturbances, severe cerebral vascular disease, and marked disability due to other illness.

Selection of the therapeutic agent for a particular patient is discussed by Spittel, who emphasizes the need for familiarizing oneself with the different groups of antihypertensive drugs at our command. Combination of several drugs enables one at times to obtain an additive effect while minimizing undesirable side effects. Juergens deals with the side effects of the various antihypertensive drugs in common use, and their efficacy is carefully evaluated by Gifford. Without minimizing the frequency of undesirable reactions of the effective drugs, Juergens stresses the essentially benign nature of most of these side effects. Only occasionally is it necessary to discontinue the drugs altogether, and frequently the intensity of the reactions decreases with time. He rightly emphasizes that patients do not die of constipation or dry mouth or blurred vision or impotence, but they do die of uncontrolled hypertension. Though not curative, antihypertensive treatment has been

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reported to bring about a 50% five-year survival in malignant hypertension compared with 1% in the untreated group of Keith, Wagener and Barker. Striking improvement in congestive heart failure due to hypertension has been a regular feature of treatment, enabling one quite often to abandon digitalis therapy.

General considerations of antihypertensive therapy by Estes conclude this brief but comprehensive symposium. Estes stresses our ignorance of the cause of essential hypertension and admits freely that present treatment of this disorder is far from ideal. Premature reports of excellent results by one or the other drug have aroused false hopes in many hypertensive patients and resulted in bitter disappointment later on. Various reasons conspire to cause patients to discontinue their program of antihypertensive therapy, and these should be reduced to a minimum. Gold, in the summary to the *Cornell Conferences on Therapy* in 1951,[1] said "It is fortunate that this conference is intended for the profession and is not likely to reach any considerable number of nonmedical readers. For the victims of hypertension, or the prospective one, it can hardly be considered a source of encouragement" (p. 250). Evidence which has accumulated in recent years and which is reflected in the Mayo Clinic symposium justifies the adoption of a much less pessimistic attitude towards hypertension, and should encourage a more positive approach towards the treatment of this disorder.

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INSECTICIDE RESISTANCE

Insects and other arthropods are important as sources and as vectors of human disease. The role of the mosquito in malaria, yellow fever, dengue, certain forms of encephalitis, and filariasis has become a by-word in medicine. When the synthetic insecticides were employed during the last war, the reduction in the incidence of malaria and of typhus in the Mediterranean area was dramatic. For malaria in particular, there appeared to be hope of achieving control of this disease, which for centuries had caused countless illnesses and deaths in widespread areas of the world. The first materials used were the chlorinated hydrocarbons known as DDT and BHC. Others were quickly added, together with a new group of synthetic materials – the organic phosphorus compounds.

In 1946 resistance to DDT in one species was noted. This resistance has developed rapidly to the point where there are now at least 40 arthropod species of public health importance which exhibit resistance to insecticides. With this discovery, the hope of easy control of these diseases diminished.

Resistance to chlorinated hydrocarbons has resulted in the abandonment of some of these materials for the control of houseflies and fly-borne diseases. Resistance of mosquitoes to DDT and other chlorinated hydrocarbons has reached the stage where control measures are not effective in some areas. Cockroaches show resistance to Chlordane in many parts of the United States. Resistance of bedbugs to DDT has been noted all over the world. Evidence of resistance of fleas, lice and ticks is available from widespread areas. More recently some species have shown resistance to the organic phosphorus compounds.

This development of resistance to insecticides has caused concern because of their public health importance in disease and in vector control. It may reduce public confidence in domestic spraying for vector control. Because of this the World Health Organization appointed Professor A. W. A. Brown, from the University of Western Ontario, to give full-time attention to this problem. In an article published recently, Dr. Brown has summarized developments during 1956 and 1957.[1]

In general there are two types of resistance to chlorinated hydrocarbon insecticides: (1) resistance to DDT and its analogues (such as TDE and Methoxychlor); and (2) resistance to cyclodiene compounds (such as Chlordane, Aldrin, Dieldrin, Endrin, and Toxaphene) and to BHC.

Resistance to either of these types confers a degree of cross-resistance to other members of the same group. In the case of DDT, physiological studies indicate that resistant houseflies detoxify it by a special enzyme called DDT-dehydrochlorinase. Secondary factors may be involved such as a higher fat content, a higher content of cytochrome oxidase, or a heavier cuticle in the resistant strain. With BHC-resistant varieties there is decreased absorption of the toxin and increased rate of detoxification. Resistance mechanisms with the cyclodiene compounds are as yet not understood.

Genetic studies indicate that a single gene is involved in the detoxification mechanism. The insecticides do not produce mutations, but they induce resistance by selecting insects of a certain genetic type. When the use of an insecticide is discontinued, resistance persists for many generations but gradually decreases, owing to interbreeding with unexposed and therefore unselected insects. In addition, there has been described an extra vigour of the strain, which is polygenic and which has been termed "vigor tolerance" in the American literature.

The matter of insecticide resistance is of real concern because of its public health significance. Resistance in some strains is being acquired faster than measures to overcome it can be taken. Substitute insecticides of proven effectiveness may be kept in readiness for use as a counter-measure when resistance first appears. In this connection, the World Health Organization can assist in the detection of local resistance and can make recommendations on substitute control measures. The report mentioned above indicates that some new compounds give promise of selected action against resistant strains.

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NEW LIGHT ON PATELLECTOMY

There has been considerable controversy as to the function which follows patellectomy, but it now seems that long-term results do not warrant the optimism of a few years ago. The majority of patients on whom patellectomy is performed complain of a dull ache in the knee joint, aggravated by long periods of walking or standing and often associated with a sense of instability. Observations such as these fail to support the premise propounded by Brooke, and supported by Watson-Jones, that the function of the knee joint is enhanced by the absence of the patella, which Brooke believed to be in the process of phylogenetic reduction. It would therefore appear that, if possible, the patella should be salvaged, because it offers a certain degree of protection to repeated abnormal stresses and strains.

Studies were conducted by De Palma and Flynn (*J. Bone & Joint Surg.*, 40A: 395, 1958) in three groups of dogs, depending on whether the medial half of the dog's patella was removed, the entire patella, or the upper or lower half. The animals were destroyed and joint changes assessed at intervals of from 23 to 338 days, after clinical and radiographic evaluation had been attempted. Severe changes were not observed until approximately five months had elapsed. However, early after partial patellectomy, thickened fibrous tissue was lined by clusters of synovial villi forming a pannus which extended over the medial margin of the remaining portion of the patella. Grossly this remained normal, although the adjacent portion of the quadriceps tendon had assumed the characteristics of fibrocartilage.

At forty days, changes minimal in intensity were discernible in the articular cartilage of the lateral femoral condyle, but no response of the subchondral bone in the form of marginal osteophytes was noted at this stage of the investigation.

By 188 days extensive changes were noted, with fraying, pitting, and fibrillation of the remaining portion of the patella adjacent to the cut surface. Marginal osteophytes were observed on the anterior surface of the lateral femoral condyle. Chondro-osseous excrescences were noted also in the intercondylar surface. It was obvious that the articular surface of the femur, which came in contact with the irregular rough tissue in the patellar bed, responded in a manner consistent with hypertrophic arthritis.

By 261 days the changes were much more advanced and, on either side of the piece of remaining patella, two large concave areas of tough, fibrocartilaginous tissue with a smooth, glistening articular surface had formed in the lateral expansions of the quadriceps apparatus. The anterior articular surface of the femur was pitted and contained several irregular chondro-osteophytes.

By 280 days after hemipatellectomy the remnant of the patella was incorporated in an irregular mass of new tissue with the consistency of bone. The articular surface of the patella was completely devoid of cartilage. The anterior surface of the femoral condyle was increased in width because of large, irregular, marginal excrescences. Large, tough, fibrous adhesions completely covered the articular surface of the anterior aspect of the femur.

From these observations it is concluded that any disturbance in the normal mechanism of the knee joint is conducive to the production of regressive changes in the soft tissues and in the cartilaginous and osseous components of the articulation.

As in hemipatellectomy, total excision resulted in a swollen joint and periarticular induration. The capsule was found to be thickened and œdematous, with light brownish discoloration of the synovial membrane. It appeared that the synovial membrane was impregnated with broken-down blood pigments. Other hyperplastic changes with eburnation of the articular margins were noted. In some specimens the patellar bed had been converted into a smooth gliding organ producing no deleterious effects on the femoral side of the joint. It is considered that this might be a temporary change which, with continuous function, eventually breaks down and is replaced by a patellar bed with a rough, irregularly scored surface in which fragments of fibrocartilage are demonstrable. Later specimens constantly revealed irregular areas of cartilaginous and bony consistency in the patellar tendons in addition to pronounced thickening and striation. In one of the many fine photographs taken 72 days after total excision, the entire patellar bed exhibits marked overgrowth of fibrous tissue and grape-like clusters of synovial villi. The articular cartilage of the femoral condyles is thin and pitted.

In the third group in which either the superior or inferior pole of the patella was excised, the animals had little or no disability from the time following the operation to the date of sacrifice. Several months later changes similar to those in the other groups were evident, but these alterations never equalled those noted in the animals in which a hemipatellectomy had been performed. The changes, however, seemed to be gradually progressive, so that in a long period of time they might reach such magnitude as to produce varying degrees of dysfunction.

Although these changes are noteworthy and the pathodynamics probably comparable, it does not necessarily follow that the changes observed in humans will be precisely those noted in these dogs. The differences in anatomical construction of the knee joint of the dog and that of man preclude accurate assessment of the severity of such alterations. It is concluded that, whenever possible, the patella, or at least its superior or inferior pole, should be preserved, and that in those instances in which excision appears mandatory, new methods should be designed whereby the normal mechanics of the joint are restored. ALLAN M. DAVIDSON

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ERRATUM: FINALGON–THERMAL MODIFICATIONS

The authors of the Short Communication published on page 44 of the July 1 issue are Jean Rousseau, M.D. and Rita Gagne Desrosiers, M.D.

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Medical News in brief

LAMINAR EXCISION FOR SPONDYLOLYSIS

Because there is some evidence that the backache and pain in the legs in cases of spondylolysis and spondylolisthesis are due not to instability of the lumbo-sacral joint, as has been generally believed, but to abnormal mobility of the unattached lamina, Todd and Gardner (*Surg. Gynec. & Obst.*, 106: 724, 1958) have operated upon 15 patients by simple excision of the unattached lamina. Results were surprisingly good in a follow-up period of 20 to 36 months. All patients had complained of pain in the back and legs, and neurological findings had been variable, sometimes showing obvious nerve root compression and sometimes nothing. Only one patient had a poor result from the operation; seven had excellent and four good results.

RADIATION HAZARDS OF INTRAVENOUS PYELOGRAPHY

A review of the records of 200 patients who had undergone intravenous pyelography revealed that about one out of every four pyelograms was unnecessary and could have been avoided if the clinicians had observed more carefully certain indications. During intravenous pyelography in adults, studies indicate that the ovaries probably receive doses of less than one roentgen while the testes often receive several roentgens. The amount of radiation to the gonadal regions can be appreciably decreased without interfering with the diagnostic accuracy of the examination. A piece of lead or lead rubber may be used to cover the testes in the male patient and the same may be employed to cover the lower half of the abdomen in the female patient.—I. Van Woert Jr. *et al.*: *J. A. M. A.*, 166: 1826, 1958.

PLACEBO EFFECTS IN PSYCHIATRY

In an Oslo hospital, Lehmann and his colleagues (*Tidsskr. norske laegefor.*, 78: 588, 1958) carried out a double blind study of one of the newer phenothiazines, acepromazine, which had been said by French observers to have a favourable effect in various neuroses and psychoses. A total of 97 patients (neurotics, psychotics, alcoholics and others) admitted to a psychiatric observation ward were included in the experiment. Results showed that 3 out of 56 patients treated with the placebo improved as against one treated with acepromazine.

The main interest of the paper lies not in the negative results with the drug, but in the remarkably low placebo effect obtained. The authors analyze the factors affecting a placebo action and advance as causes for their low incidence (1) the fact that the active substance was not effective, so that patients on placebo were not influenced by the improvement of others around them; (2) the severe criteria of improvement which they had adopted; (3) the fact that so many of their patients had been treated outside hospital with other drugs without success. They had therefore come to expect failure.

PENICILLINASE IN THE TREATMENT OF PENICILLIN REACTIONS

Becker (*Ann. Int. Med.*, 48: 1228, 1958) has treated penicillin reactions in 46 patients with penicillinase. Twenty-four were treated with intramuscular penicillinase alone, with uniformly good results. The other 22 had previously received concomitant therapy with various antihistaminics or with corticotropin and corticosteroids. In 20 of these the favourable clinical response seemed to be directly attributable to the penicillinase. In the two cases with a poor response the penicillinase was given weeks to months after the onset of the penicillin reaction.

No systemic toxic reactions to penicillinase were noted. A few patients complained of pain at the site of injection, and one patient had a local reaction with induration which may or may not have been due to the enzyme. Penicillinase should prove an extremely valuable adjuvant in treatment of penicillin reactions.

CLINICAL EXPERIENCE WITH ORALLY ADMINISTERED WARFARIN SODIUM

Danford, Juergens and Barker (*Proc. Staff Meet. Mayo Clin.*, 33: 359, 1958) report their experience with orally administered warfarin sodium in 170 hospitalized patients and compare its action with that in 100 similar patients on dicoumarol therapy.

The initial dose of 40-60 mg. of warfarin was about as effective as the initial combined doses of tromexan and dicoumarol, producing therapeutic levels of hypoprothrombinæmia in 12 to 24 hours in 45% of the patients and in 36-48 hours in 95% of patients. Although 14% of the warfarin-treated and 24% of the dicoumarol-tromexan treated showed at some time during the first 72 hours extremely low prothrombin levels, they rarely experienced bleeding manifestations and in all only three patients needed vitamin K preparations. No other untoward effects were observed from warfarin sodium therapy, and the authors conclude that it possesses modest advantages over dicoumarol as an anticoagulant.

CORTISONE TREATMENT OF VITAMIN D INTOXICATION

Verner *et al.* (*Ann. Int. Med.*, 48: 765, 1958) report two cases of vitamin D intoxication occurring in elderly adults presenting clinical syndromes of mental confusion, dehydration, polyuria and hypokalæmic alkalosis. Each had received intoxicating doses of vitamin D from druggists without a physician's prescription. Cortisone therapy resulted in improved mental status in 48 hours, and return of serum calcium to normal in eight and 13 days, respectively.

It is stressed that the uræmia of hypervitaminosis D is a reversible process, and that untreated cases may progress to death in renal failure with metastatic calcification. The prompt restitution of normal serum calcium levels by cortisone administration appears to favour a more rapid resolution of uræmia in these patients.

(Continued on advertising page 45)

MEDICAL FILMS

CONTINUING the listing of available films on medical and related subjects, we list below additional films. The films are held in the National Medical and Biological Film Library and are distributed by the Canadian Film Institute, 142 Sparks Street, Ottawa, Ontario. The evaluations have been prepared by Canadian specialists in the subjects of the films, under the Medical Committee of the Scientific Division of the Canadian Film Institute, which is headed by Dr. G. H. Ettinger.

DISEASE (Pathology, Diagnosis, Treatment)

Syphilis—1942; Sound; Colour; 3 parts.

Produced for the United States Public Health Service.

Description.—An instructional-training film, designed to illustrate and encourage the diagnosis and treatment of syphilis by the general practitioner.

Appraisal (1945).—A very good film, valuable for medical students, nurses, clinical laboratory technicians and general practitioners. Part III does not consider intensive treatment of early syphilis or the use of penicillin, but is otherwise up-to-date. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (Part I: $3.00; Part II: $3.00; Part III: $4.00). For purchase apply to the U.S. Public Health Service, Washington, D.C.

Syphilitic Venereal Disease—1954; Sound; Colour; 27 minutes.

Produced for E. R. Squibb & Sons.

Description.—An instructional film, outlining the course and treatment of syphilis.

Appraisal (1956).—Recommended for medical students in the clinical years and for general practitioners; suitable for nurses. Criticisms: short physical examination sequence too cursory and implies lack of thoroughness; several points not mentioned, such as treponema immobilization tests to differentiate false positive serologic tests, and present status of use of bismuth or iodides in reducing risk of Herxheimer reaction. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($4.50). For purchase apply to E. R. Squibb & Sons of Canada Limited, 2201 Côte de Liesse Road, Montreal, P.Q.

Therapeutic Uses of Heat and Cold, Part I: Administering Hot Applications—1945; Sound; B & W; 21 minutes.

Produced for the U.S. Office of Education.

Description.—An instructional-training film, illustrating methods of applying heat as a therapeutic measure, and the underlying principles and results.

Appraisal (1945).—A clear, concise presentation; animation very good; techniques accurate and well carried out. Recommended for professional nurses and suitable for certain lay groups.

Availability.—National Medical and Biological Film Library ($3.00). Purchase from United World Films Inc., 1445 Park Avenue, New York 29, N.Y.

PHARMACOLOGY

Birth of a Drug—1949; Sound; B & W; 35 minutes.

Produced for Imperial Chemical (Pharmaceuticals) Limited.

Description.—An interpretive-instructional film, presenting the story of modern drug development.

Appraisal (1952).—A very well produced film, particularly good for medical students in the pre-clinical years, pre-medical students and general scientific audiences. Suitable for other medical groups, graduate and undergraduate, and for interested lay audiences.

Availability.—National Medical and Biological Film Library ($3.00). For purchase apply to the Publicity Department, Imperial Chemical (Pharmaceuticals) Limited, Fulshaw Hall, Wilmslow, Manchester, England.

OBSTETRICS AND GYNÆCOLOGY

The Appraisal of the Newborn—1939; Sound; B & W; 20 minutes.

Produced by the Bureau of Visual Instruction, University of Wisconsin.

Description.—An instructional-training film, illustrating the importance and the technique of thorough medical examination of the newborn infant.

Appraisal (1945).—A very well done film, with sound principles. Recommended for medical students, interns, general practitioners, specialists in obstetrics and pædiatrics, and nurses. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($3.00). For purchase apply to the University of Wisconsin Photographic Laboratory, 1208 Johnson Street, Madison, Wisconsin.

Childbirth Without Fear—1953; Sound; Colour; 20 minutes.

Produced in South Africa for Dr. Grantly Dick Read.

Description.—Narrated by Dr. Read, who appears in the film, this is a record of three "natural childbirth" deliveries.

Appraisal (1956).—An excellent presentation of the cause to which Dr. Grantly Dick Read has for many years devoted his efforts, and a good presentation of delivery for prepared women. Essentially a film for the medical profession, for those who know Dr. Read's teachings, for medical students in the clinical years, and for nurses. It may also be shown by obstetricians practising natural childbirth to patients who wish to see it and who the doctor feels may benefit by it. *Unsuitable for non-medical audiences,* except as indicated above.

Availability.—National Medical and Biological Film Library ($4.00). Purchase from J. Arthur Rank Film Distributors (Canada) Limited, 277 Victoria Street, Toronto, Ontario.

A Concept of Maternal and Neonatal Care—1951; Sound; B & W; 26 minutes.

Produced by George Washington University Hospital and School of Medicine in cooperation with the Medical Audio-Visual Institute of the Association of American Medical Colleges.

Description.—An interpretive-training film, illustrating an over-all program for the care of mother and newborn infant, the highlights of which are prenatal and postnatal patient education and the "rooming-in" concept of hospital care during the neonatal period.

Appraisal (1952).—A very good film. Being a report to the profession on a way of practice found in some maternity hospitals, its value as a purely "instructional" film is limited. Hospital layout and facilities shown are as yet rare in this country, and the film should be effective in bringing this new concept to the attention of those planning hospital construction. Will have its greatest value as a discussion springboard for professional groups. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($3.00). For purchase apply to Medical Audio-Visual Institute, Association of American Medical Colleges, 185 North Wabash Avenue, Chicago 1, Illinois.

Contraceptive Methods and Technique—1935; Silent; B & W; 32 minutes.

Produced by Marie Pichel Warner, M.D., New York, N.Y.

Description.—An illustration of various types of contraceptive materials and methods of their use. The film is mounted on two separate reels, for independent showing if desired. Reel I lists and evaluates the various contraceptive methods. Reel II presents clinical demonstrations of the fitting and the instruction of patients in the use of vaginal occlusive diaphragms.

Appraisal (1945).—Recommended for medical students in the final years, interns, general practitioners and gynæcologists. A good teaching medium, with the various materials in general use and the methods of application clearly presented. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($3.00). For purchase apply to Marie Pichel Warner, M.D., 20 West 86th Street, New York, N.Y.

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Craniotomy on a Dead Fetus – 1930; Silent; B & W; 48 minutes.

Produced by the late Joseph B. DeLee, M.D., Chicago Lying-In Hospital.

Description.—An instructional film, illustrating the technique of craniotomy on the dead fetus, in brow and breech presentations. The technique of operation is demonstrated in the case of a primipara, aged 46, fetus dead and macerated, brow presentation.

Appraisal (1945).—Recommended for senior medical students, interns, general practitioners and obstetricians. A good film to demonstrate craniotomy, although this procedure is not nearly so common as in past years. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($1.50). For purchase apply to Sol T. DeLee, M.D., 6909 S. Cregier Avenue, Chicago 49, Illinois.

Eclampsia—1939; Silent; B & W; 48 minutes.

Produced by the late Joseph B. DeLee, M.D., Chicago Lying-In Hospital, with the assistance of Wm. J. Dieckman, M.D.

Description.—An instructional film, dealing with the prevention and treatment of eclampsia.

Appraisal (1945).—This film is invaluable—one of the best medical films seen to date. Subject has been excellently treated, clearly presented and covered in every phase. Demonstration of the clinical course is up-to-date, although some methods of treatment have been changed. Recommended for senior medical students, interns, practitioners and nurses. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($4.50). For purchase apply to Sol T. DeLee, M.D., 6909 S. Cregier Avenue, Chicago 49, Illinois.

Episiotomy and Repair—1932; Silent; B & W; 51 minutes.

Produced by the late Joseph B. DeLee, M.D., Chicago Lying-In Hospital.

Description.—An instructional film, demonstrating the anatomy of the pelvic floor with reference to areas involved in episiotomy, the actual operation of episiotomy, and the technique of its repair.

Appraisal (1945).—A first-class film, recommended as a teaching aid for senior medical students, interns, and nurses. Despite its age, the techniques are sound and up-to-date, with a few small and relatively unimportant exceptions. Also suitable for general practitioners and obstetricians. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($4.50). For purchase apply to Sol T. DeLee, M.D., 6909 S. Cregier Avenue, Chicago 49, Illinois.

Fetal Birth Injuries—1936; Silent; B & W; 67 minutes.

Produced by the late Joseph B. DeLee, M.D., Chicago Lying-In Hospital.

Description.—An instructional film, illustrating various injuries of the newborn, with preventive procedures and treatment.

Appraisal (1945).—A very fine film and definitely recommended for senior medical students, interns, general practitioners and obstetricians. It covers every aspect of the subject; all pathological lesions are most clearly shown. Despite the film's age it is thoroughly up-to-date. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($6.00). For purchase apply to Sol T. DeLee, M.D., 6909 S. Cregier Avenue, Chicago 49, Illinois.

The Forceps Operation and Episiotomy—1934; Sound; B & W; 64 minutes.

Produced by the late Joseph B. DeLee, M.D., Chicago Lying-In Hospital.

Description.—An instructional film, illustrating the principles and use of the obstetrical forceps, the techniques of forceps delivery and of episiotomy and its repair.

Appraisal (1945).—An exceptionally good film, very thoroughly presented, for teaching students or for use in postgraduate instruction. Recommended for senior medical students, interns, general practitioners and obstetricians. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($7.50). For purchase apply to Sol T. DeLee, M.D., 6909 S. Cregier Avenue, Chicago 49, Illinois.

The Human Cervix in Health and Disease—1943; Silent; Colour; 21 minutes.

Produced by Norman F. Miller, M.D., Professor of Obstetrics and Gynecology, University of Michigan.

Description.—An instructional-record film, illustrating benign and malignant lesions of the human cervix.

Appraisal (1945).—An exceptionally well done film; clinical material, photography and subtitles all excellent. Highly recommended for medical students in the clinical years and all medical and nursing audiences. While introductory subtitles indicate that the film was prepared for lay groups, its use in public health work is not considered a sound policy—the film is too gruesome for lay education. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($3.00). For purchase apply to Norman F. Miller, M.D., University of Michigan Hospital, Ann Arbor, Mich.

LABORATORY TECHNOLOGY

Career: Medical Technologist – 1954; Sound; Colour; 24 minutes.

Presented by the National Committee for Careers in Medical Technology, and sponsored by the American Society of Clinical Pathologists, the American Society of Medical Technologists, and the College of American Pathologists.

Description.—A recruitment film, designed to provide high school students and the lay public with an introduction to the work of the medical laboratory and, in particular, to the work of the medical laboratory technologist.

Appraisal (1954).—Portrays extremely well the potential interest in laboratory work for those whose school interest leans to science and mathematics. Deals naturally with U.S. educational requirements, but a Canadian trailer has been added noting differences in educational requirements between the two countries. Should preferably be presented by professional person capable of introducing it and answering questions. Recommended for high school and college groups and any interested medical audiences.

Availability.—National Medical and Biological Film Library ($3.00). Purchase from National Committee for Careers in Medical Technology, 1785 Massachusetts Avenue, N.W., Washington 6, D.C.

Venepuncture—1952; Sound; Colour; 14 minutes.

Produced by the I.C.I. Film Unit, for Imperial Chemical Industries Limited. Prepared in the Bacteriology Department, St. Mary's Hospital Medical School, London, England.

Description.—An instructional-training film, demonstrating correct technique and equipment for venepuncture.

Appraisal (1953).—A well-prepared film on a small but important subject, and one which will be found most useful in the instruction of nurses, technicians, medical students and similar groups. Recommended for such audiences, and suitable also for general practitioners. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($2.25). For purchase apply to Publicity Department, Imperial Chemical (Pharmaceuticals) Limited, Fulshaw Hall, Wilmslow, Manchester, England.

What Is Cancer?—1949; Sound; Colour; 26 minutes.

Produced by Audio Production Inc., for the American Cancer Society.

Description.—An instructional-training film, designed to give junior medical and technical personnel a sound concept of cancer.

Appraisal (1949).—A very good film, recommended for nurses, technicians and medical auxiliaries, pre-medical students and medical students in the pre-clinical years. Suitable for other interested professional groups, and scientific audiences.

Availability.—National Medical and Biological Film Library ($6.00). Purchase from American Cancer Society Inc., 47 Beaver Street, New York 4, N.Y.

(To be continued)

Men and Books

PIONEERS OF MEDICINE IN NEWFOUNDLAND

In Newfoundland, the name of Dr. William Carson is a household word, mainly because of his fight to obtain representative government for Newfoundland. At the annual dinner of the Newfoundland Council of the Canadian Medical Association, held in Corner Brook in July, Dr. Cluny Macpherson of St. John's gave the members copies of an interesting document in which Charles H. Renouf was apprenticed to Dr. Carson and his brother, Dr. Samuel Carson. Renouf, who was born in 1816 and died in 1878, became indentured to the Carsons in 1831 and finished his apprenticeship in 1836. He went to Edinburgh, where he obtained the F.R.C.S.(Edin.) of the Royal College of Surgeons of Edinburgh on May 15, 1839.

The indenture, which is now in the possession of Dr. William Carson's grandson, the Hon. R. B. Job, reads as follows:

"THIS INDENTURE made at St. John's in the Island of Newfoundland this first day of January in the year of our Lord one thousand eight hundred and thirty-one between Charles H. Renouf of St. John's, Newfoundland, of the one part, and William and Samuel Carson of St. John's aforesaid, Doctors in Medicine, of the other part—witnesseth that the said Charles H. Renouf of his own free will and accord testified by his sealing and delivering these presents hath put and bound himself apprentice to the said William and Samuel Carson to be taught and instructed in the practice and profession of a surgeon and apothecary from the day of the date of these presents until the first day of January, one thousand eight hundred and thirty-six, making a term of five years from the first day of January now last past. When under agreement for these Indentures the said Charles H. Renouf entered the service of the said William and Samuel Carson, and the said William and Samuel Carson agreed to take and accept the said Charles H. Renouf as their apprentice during the said term, and the said Charles H. Renouf doth hereby convenant, promise, and agree to and with the said William and Samuel Carson their executors and administrators that the said Charles H. Renouf shall and will during the said term faithfully and truly serve the said William and Samuel Carson as an apprentice in the said profession and business of surgeon and apothecary, and diligently attend to the business of the said William and Samuel Carson strictly keeping their secrets and the secrets of their patients and doing no damage or injury to his said masters nor knowingly suffering the same to be done by others without acquainting his said masters therewith, but shall and will in all respects acquit and demean himself as an honest and faithful apprentice, and said William and Samuel Carson do hereby for themselves, executors and administrators in like manners (that is to say) that they the said William and Samuel Carson, according to the best means in their power, during the said term teach and instruct the said Charles H. Renouf in the several arts of Medicine, Surgery and Pharmacy, and in the practice and profession of surgeon and apothecary and in all things whatsoever belonging thereto, and also that the said Charles H. Renouf shall have the full benefit and advantage of attending all surgical operations performed in the practice of the said William and Samuel Carson and further during the said term the said William and Samuel Carson shall find the said Charles H. Renouf suitable and convenient lodgings in the house of the said William Carson and board at their table, and moreover that they will and truly pay or cause to be paid in money to the said Charles H. Renouf for the third, fourth and fifth years respectively of the said term the sum of twenty pounds for one and each of the said three years, to be paid and payable in currency on the first day of January in each year, the first payment of twenty pounds to be made on the first day of January, one thousand eight hundred and thirty-four—and for the true performance of all the covenants and agreements herein contained, each of the said parties doth bind himself unto the others of them by these presents. In Witness whereof the said parties to these Indentures interchangeably have set their hands and seals, in Saint John's, Newfoundland, the day and year before written.

(Signed) CHARLES H. RENOUF

Signed, Sealed and Delivered
in the presence of

WILLIAM CARSON
SAMUEL CARSON
HENRY H. STABB

St. John's, Newfoundland,
February 8th, 1836.

We certify that Charles H. Renouf has completed the full term of his apprenticeship being much to our satisfaction. He was attentive, intelligent and steady.

(Signed) WILLIAM CARSON, M.D.
SAMUEL CARSON, M.D.

GENERAL PRACTICE

PERSONALITY FACTORS IN THE HEALING PROCESS*

B. H. McNEEL, M.D.,† *Toronto*

THE MODERN PHYSICIAN who finds that his public expect him to have a wonder drug or a formula of some sort to cure every ill may well wish that he were able to share responsibility for healing with some other agency. He may well look back to the modest assertion of Ambroise Paré: "I dress the wound, God heals it", or to the centuries-old but recently neglected concept of the "vis medicatrix naturæ"—the healing power of nature.

For some time we have been returning to a renewed emphasis on the defensive and recuperative powers resident in the human organism. We see, however, that the healing power of nature varies in potency from individual to individual, and in the same individual from time to time. Though it resides in the organism as an intrinsic quality, it is not independent of the environmental situation. Moreover, it is not the only intrinsic quality that governs the organism's response to pathogenic agents, for there are also those internal factors that may foster disease and predispose to destruction.

It is easy to see that therapeutic efforts may be directed towards: (1) the employment of direct

*Address to Annual Meeting of the Medical Advisory Section, Ontario Tuberculosis Association, Toronto, Ont., October 31, 1957.

†Chief, Mental Health Division, Ontario Department of Health, Toronto.

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means to remove, destroy or inactivate the pathogenic agent, and (2) the employment of means to stimulate and foster the defensive and recuperative powers of the organism.

In the first instance, we assume that the patient will be the passive recipient of our ministrations, and in the second instance, we assume that biologically and psychologically he will be the active participant in the healing process. In the event that either assumption proves incorrect, we do not usually view the new problem as a therapeutic challenge but attribute it to either the psychological or biological incorrigibility of this particular human organism.

A considerable proportion of therapeutic effort is ineffective because (a) action against the pathogen cannot be carried out, or (b) conditions that inhibit the defensive and recuperative powers are not overcome. Failures due to these causes may be attributed to personality factors. If we accept the doctrine of the essential unity of the individual, we should include in this term constitutional and biological as well as psychological and social factors. However, for the purpose of this paper we will use the term personality in the more restricted sense of "psychosocial". Undoubtedly, in determining the effect of treatment, the attitude of the patient plays a part. Perhaps there is a pathological dependency fostering invalidism, perhaps a subconscious wish for self-destruction, or an emotional deficiency which leaves the patient without a positive drive toward health.

Attention to personality factors may help in the healing process in two ways: (1) by ensuring the patient's co-operation in the treatment program; (2) by influencing attitudes and feelings which affect the healing process.

I think it would be safe to say that from the beginning of the scientific age until World War II, medical thought gave little credence to older ideas of the relationship of psychic and physical events. The love-sick maid, who languished away, undoubtedly died of tuberculosis, and it was only by poetic licence that her demise could have been attributed in any way to her state of mind. However, there are romantics even among physicians, and occasionally most of us have heard some old colleague say that his patient died simply because he no longer had the will to live. In cases where the conclusion was inescapable that psychic and physical events were related, as for example in conversion hysteria, the connection was attributed in a vague sort of way to the power of imagination.

Increasing knowledge of general physiology and neurophysiology, and of their disturbances, gradually made it clear that a system of pathways exists between the brain, the endocrine glands, and all the organs of the periphery that could explain how cerebral events and somatic events might be associated. From Cannon to Selye, there has been progressively developed an understandable picture of the means by which physical events are related to psychic events. Cannon demonstrated that the chemical and cellular constituents of the blood are altered during intense emotional experience, and postulated that these changes are mediated by the autonomic nervous system and the endocrine glands. These findings were further elaborated by the discovery of the role of the hypothalamus in metabolism and in the vital rhythmic activities of the body. A chain of relationships between emotional disturbance, neurocirculatory changes, local nutritional changes, and finally, local structural changes in the stomach and other organs was clearly established. The archipallium which had been thought of as vestigial turned out to be a part of the vitally important visceral brain, with functions closely related to emotional experience. Selye, in his work on the general adaptation syndrome, indicated that severe psychic stress and physical stress have common results, and his work gives credence to the possibility, which many of us have doubted, that a human being may actually be scared to death.

If psychic stress and physical stress have common effects on the organism, then one would expect the effects of the two acting together to be additive. In a very anxious patient suffering from tuberculosis, the systemic effect would be the resultant of the effect of severe anxiety plus the effect of tuberculous disease.

To complete the picture we must mention the converse of our earlier discussion, namely, that physical illness results in some degree of personality disturbance. This may be the mild disgruntlement that accompanies a head cold, or may be something more profound. The psychic disturbance may be related to the meaning of the illness to the person—loss of independence, removal from security of home and family, threat of long-term incapacity, threat of death, and various other unacceptable meanings. Or, on a simpler biological level, it may be part of a total reaction to impairment of a vital function, e.g. anxiety precipitated by interference with breathing.

Discussions of psychosomatic medicine usually lead to the question "Is it possible to correlate specific disease syndromes with specific personality types?" Though we are not now engaged in a discussion of epidemiology, we should at least acknowledge the question. In the last 75 years at least, there have been periodic attempts to link specific diseases to specific personality types. In earlier years, this was attempted on a constitutional basis, e.g. a parallelism was drawn between asthenic body build, schizophrenia, and tuberculosis. In recent years, we have had a few outstanding contributions, such as Sheldon's, to the constitutional approach to personality structure. However, the great effort in this period has been directed to the correlation of disease and personality structure on a psychodynamic basis, i.e. attempting to correlate specific physical syndromes with specific psychic conflicts. As a result, we have such concepts as the peptic ulcer personality and the hypertensive personality. These concepts have received wide recognition but not complete acceptance. The symbolic relationship of physical symptoms to psychic disturbance is of course more apparent in those conditions which arise solely from an internal disturbance of function than in conditions which arise in response to an invading pathogen, as in tuberculosis.

Most of the phenomena which we have discussed above are examples of the disruptive effect of disturbed emotion. Unfortunately the converse, the constructive effect of Norman Vincent Peale's

"positive thinking", has not been demonstrated in the clinical field with equal clarity. Cannon made a beginning in his reference to the anabolic functions of the parasympathetic system, but we do not have evidence of a state of super-wellbeing induced by healthy-mindedness comparable to the evidence of psychosomatic illness. Part of the reason for this lack may be that, the human situation being what it is, we have more opportunity to observe the effects of fear, frustration, resentment and guilt than to observe the result of faith, hope, love and enthusiasm.

Whether or not we have proper "scientific" confirmation, we have a long tradition attesting to the therapeutic efficacy of constructive attitudes and feelings. This goes at least as far back as the assertion in the Book of Proverbs, "A merry heart doeth good like a medicine." Perhaps one should not use such a reference without some definition, since words like "merry" may be counterfeit currency. By way of explanation I would only draw your attention to a description of a scene by a modern writer who said, "I have seldom seen so much gaiety and so little happiness."

Suppose we accept the proposition that there are factors in personality, or let us say psychosocial factors, that influence the healing process positively or negatively, what practical use can we make of this appreciation? I think that we have not yet developed the skill to use it fully, although some happily endowed individuals may be exceptionally able to do so.

Since, in the field of tuberculosis, your first level of competence is in physical treatment, the first aim in the psychosocial sense is to have the patient undertake a treatment program and continue with it until the desired result has been obtained.

Perhaps the first step in gaining the required co-operation is for us to discard the idea that any fool can see that this is for the patient's good, and therefore that any patient, whether wise or foolish, can be expected to co-operate without further ado. We have to accept the fact that many if not all patients will, to a greater or less degree, show some evidence of misunderstanding, apprehension, or resentment. These are conditions which can interfere with the program, and which must be recognized and resolved if possible by the therapeutic staff.

There are two approaches to the resolution of the difficulties, and it may be necessary to employ both. First, there is the manipulation of the environment. We use this method when we attempt to make the treatment setting as congenial as possible, and again when we attempt by social service or other means to minimize the environmental pressures that draw the patient away from treatment. In employing such measures, we are influencing the patient's attitudes and feelings indirectly. It may also be necessary at times to undertake a more direct approach by an open discussion of his attitudes and feelings, or in some instances, by formal psychotherapy under psychiatric auspices.

Probably the most obvious evidence of a breakdown of patient participation is the irregular discharge. A careful study of irregular discharges should reveal many features of the environment and of personal adjustment that contribute to treatment failures, and conversely, those that might be more effectively employed to achieve therapeutic success. The book "Personality, Stress, and Tuberculosis", edited by Dr. Sparer, contains several studies on irregular discharges. A committee of the Medical Section of the Ontario Tuberculosis Association, in co-operation with the Division of Tuberculosis Prevention of the Department of Health and the sanatoria, has also undertaken a study of this subject. By actively participating in studies of this type, the professional staffs of hospitals and in the field will soon enlarge their awareness and appreciation of the role that psychosocial factors play in the therapeutic program and in the healing process.

In the foregoing, only passing reference has been made to the deep-seated psychic disturbances which require expert psychiatric care. In some of these cases, specific conflicts contribute to chronic physical invalidism, and in such cases one might venture to say that tuberculosis meets a psychic need. In others, the coexistence of tuberculosis and psychiatric disorder could be considered purely coincidental, and these patients may recover from tuberculosis on routine physical treatment as quickly as any other patients. The problem of the chronic psychotic patient with tuberculosis is a special one because of the additional supervision which he requires to ensure consistent medication, adequate nutrition and satisfactory hygienic practices. However, this is a problem of hospitals which care for the tuberculous mentally ill.

In closing, I would like to refer again to the promotion of positive, dare I say "radiant", health. The examples of this condition which have been given to us are literary and anecdotal. Many of them come from religious or quasi-religious literature. From the scientific point of view, the field is practically unexplored. Any cautious clinician would be hesitant to make a statement and probably equally hesitant to attempt to experiment in this field, particularly if he were concerned about his status as a scientist. Being about as cautious as my neighbour, I would hesitate to say more, but I would like to leave you with a note of wonder.

MYASTHENIA GRAVIS

Careful clinical appraisal and response to anticholinesterase remain the basis for diagnosis in most cases of myasthenia gravis. Sometimes in very mild or equivocal cases, a provocative test with quinine or curare may be useful, but requires certain precautions. Though the pathophysiology of this disease is now better understood, the etiology remains obscure. New drugs and newer methods of administration (particularly as multiple-dose, slow-release tablets) offer much in the management of the symptoms of myasthenia gravis. The exact relationship of myasthenia gravis to the thymus and other endocrines remains obscure.—J. M. Oppentheim: *Am. J. M. Sc.*, 236: 107, 1958.

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POSTGRADUATE COURSES FOR GENERAL PHYSICIANS

Title of Course	Location	Dates	Fees
CANADA:			
Third Annual Scientific Convention, College of General Practice of Canada	Royal York Hotel, Toronto, Ontario	Monday to Thursday, April 20 - 23, 1959	
ALBERTA:			
Alberta Chapter Annual Scientific Convention	Banff Springs Hotel, Banff, Alta.; Dr. H. A. Lloyd, Edmonton, Chairman of Alberta Chapter	January 28 - 30, 1959	
ONTARIO:			
Medical Alumni Association Meeting: "Recent Advances in Diagnosis"	University of Toronto, Toronto 5	October 22 - 24, 1958	
Essex County Chapter Clinical Day	Prince Edward Hotel, Windsor; write to: Dr. A. K. Carter, Windsor, Chairman	November 5, 1958	
Metropolitan Toronto Chapter: Clinical Days	St. Joseph's Hospital Northwestern General Hospital	November 12, 1958 November 27, 1958	
Medical-Dental Seminar on "Hypnosis"	Sheraton-King Edward Hotel, Toronto; write to: Miss Pat McFate, Registrar, 1 N. Crawford Ave., Chicago 24, Ill.	October 17 - 19, 1958	$150.00 with luncheons
Second Annual Refresher Course: "Recent Advances in Child Health"	School of Hygiene and Hospital for Sick Children; write to: Dr. A. J. Rhodes, Director, School of Hygiene, University of Toronto, Toronto 5	February 9 - 11, 1959	
QUEBEC:			
Medical Day	Hôtel-Dieu de Sherbrooke; write to: Dr. Clovis Dagneau, Medical Director	October 4, 1958	
Refresher Courses for General Practitioners	Royal Victoria Hospital, Montreal; Miss Winnifred Rock, Postgraduate Board, Royal Victoria Hospital	November 10 - 15, 1958	$75.00
NEWFOUNDLAND:			
Refresher Course	St. John's, Nfld.; write to: Dr. Ian E. Rusted, 17 Exeter Ave., St. John's, Nfld.	October 27 - 29, 1958	
U.S.A.:			
Annual Assembly, American Academy of General Practice	San Francisco, California	April 6 - 9, 1959	
Scientific Assembly, Illinois Academy of General Practice	Sherman Hotel, Chicago, Ill.	November 3 - 6, 1958	
Interstate Scientific Assembly of the Interstate Postgraduate Medical Association	Hotel Statler, Cleveland, Ohio; Edwin R. Schmidt, M.D., Sec.-Treas., Box 1109, Madison 1, Wisconsin	November 10 - 13, 1958	$10.00 registration
Modern Laboratory Procedures and Clinical Practice	Dept. of Postgraduate Education, University of Buffalo School of Medicine, 3435 Main Street, Buffalo 14, N.Y.	October 15 and 16, 1958	$30.00
Recent Advances in Chest Diseases		October 22 and 23, 1958	$30.00
Psychiatric Problems in General Practice		October 29 and 30, 1958	$30.00
A comprehensive series of 21 postgraduate courses	Dept. of Postgraduate Medicine, University of Kansas School of Medicine, Kansas City 12, Kansas	Each course of 2 or 3 days' duration between October 13, 1958, and May 21, 1959	
BAHAMAS:			
6th Bahamas Clinical Conference	Dolphin Hotel, Nassau; Dr. B. L. Frank, Box 1718, Nassau	December 1 - 15, 1958 (9.30 to 11.00 a.m. and 6.00 to 7.30 p.m. daily)	

Cook County Graduate School of Medicine, 707 South Wood St., Chicago 12, Ill., and the New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York, have a wide range of concentrated courses.

Association Notes

THE CANADA ESTATE TAX ACT

An analysis of the principal changes in Federal inheritance taxation introduced by the new Canada Estate Tax Act, prepared and contributed by The Royal Trust Company.

PERSONS DOMICILED IN CANADA

Previous Taxation—A Duty on Succession

The Government of Canada has levied taxes on inheritances since 1941, in which year it first entered this field of taxation by imposing tax, or duty, on property passing to a beneficiary, the amount of the tax being based not only on the size of the Estate, but also on the relationship and sometimes on the age of the beneficiary, and the amount of the benefit. This was a tax on the person who inherited in respect of the succession passing to him, and was called Succession Duty. If the testator wished the tax to be charged to his Estate rather than to the individual legatee, it was necessary for him so to direct in his Will.

New Taxation—Charged Against the Estate

Under the new Estate Tax Act, the tax is levied against the Estate, rather than against the beneficiaries, and the rate of tax is determined solely by the value of the Estate. When the testator is survived by a spouse and minor children, the new Act provides for certain deductions from the taxable value of the Estate, and amounts bequeathed to charity may also be deducted. After deductions of this sort have been made, all Estates of the same value will be liable for tax at the same rate.

Provincial Succession Duty in Provinces of Quebec and Ontario

The Provinces of Quebec and Ontario are the only Provinces levying inheritance taxes in addition to the Estate Tax payable to the Government of Canada. All the other Provinces have entered into agreements with the Federal Government under which they withdrew from the inheritance tax field for the duration of the agreements, in exchange for financial compensation.

The inheritance tax in the Province of Quebec and Ontario is a Succession Duty charged against the beneficiary, as was the tax in the Federal field before the new Estate Tax Act. In certain circumstances, however, the Quebec Succession Duty Act permits Duty to be charged against the capital of the Estate even if the Will does not so provide. For example, where the income of an Estate is left to a revenue beneficiary, the Duty on such bequest may be charged to the capital of the Estate.

Coming Into Force

The new Act received Royal assent on September 6, 1958, and will come into force on a date to be proclaimed by the Government of Canada.

Reduction in Canada Estate Tax Because of Quebec or Ontario Domicile or Situs

The new Canada Estate Tax Act provides for a reduction by one-half of the tax imposed on the Estates of persons domiciled in the Provinces of Quebec and Ontario. In such estates passing to a spouse or in the direct line, this reduction largely offsets the duty imposed by the Province.

Also, in Estates of persons domiciled in the other Provinces, the new Act provides for a reduction of one-half the Federal Tax payable in respect of property situated in the Provinces of Quebec or Ontario.

Under the new Act these reductions are available whether or not Provincial Duty is paid, which was not so under the old Canadian Succession Duty Act.

Deduction of Foreign Taxes

The new Act provides that tax paid to a foreign government may be deducted from the tax payable, subject to the limitation of the deduction to the amount of tax payable under the Canada Estate Tax Act in respect of the property on which the foreign tax was paid. Under the old law, this credit has been allowed only in respect of taxes levied by countries with which Canada has entered into a succession duty agreement.

Tax on Foreign Real Estate

Previous to the new Act, foreign real estate owned by Canadians was not subject to succession duty. The new Act provides for the taxation of such real estate in the Estates of Canadians holding such property.

Pensions, Annuities and Voluntary Employee Payments

Although there is no change in the taxation of pensions and annuities, there is an important change in respect of voluntary payments by an employer to survivors of a deceased employee. Under the new Act this form of death benefit will be taxable, whereas under the old Act it is not.

Effect on Existing Wills

As has been mentioned above, under the Provincial Succession Duty Acts (Ontario and Quebec) and the old Canada Succession Duty Act, liability for duty falls on the beneficiary. In order that this would not happen, that is, in order that the tax burden would not fall on individual beneficiaries, many testators have already provided in their Wills that death duties are to be charged to the capital of the Estate. These Wills are therefore in line with the new Canada Estate Tax Act which charges the tax to the Estate, and such Wills should in this respect require no change.

On the other hand, where a testator's intention is that the tax should fall on his beneficiaries, he will not have directed in his Will that death duties are to be paid out of capital. In such Wills the effect of the new Act will be that tax will be charged to the capital of the Estate rather than against the beneficiaries as intended by the testator, so that the Will must be altered if the original intention is to be carried out.

Deductions where Widow and Children Survive

The basic exemption under the new Act is $40,000. Where a widow, or an *infirm* husband *and* a child

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TAX COMPARISONS*

		Quebec and Federal		*Ontario and Federal*		*Other Provinces Federal only*	
		Old	*New*	*Old*	*New*	*Old*	*New*
1. *All to wife*							
Estate of	100,000	13,880	11,100	14,505	11,725	11,760	6,200
	200,000	41,330	34,300	42,398	35,386	42,660	28,600
	500,000	155,980	135,650	150,355	130,025	156,960	116,300
	1,000,000	419,630	382,650	396,630	359,650	379,260	305,300
2. *Life interest to wife—age 50. Residue to 2 children under 18*							
Estate of	100,000	11,841	9,300	10,670	8,129	7,862	2,600
	200,000	34,364	31,900	31,637	29,173	28,728	23,800
	500,000	137,131	132,450	120,402	115,723	119,262	109,900
	1,000,000	388,247	378,450	324,304	314,507	316,495	296,900
3. *All to 1 brother, sister, nephew or niece*							
Estate of	100,000	25,350	21,100	27,590	23,340	18,700	10,200
	200,000	63,033	52,133	68,500	57,600	55,400	33,600
	500,000	200,084	169,784	214,750	184,450	183,500	122,900
	1,000,000	496,833	440,283	525,500	468,950	427,000	313,900
4. *All to 1 stranger or remote relative*							
Estate of	100,000	32,350	27,100	32,225	26,975	20,700	10,200
	200,000	78,700	65,800	79,700	66,800	59,400	33,600
	500,000	238,000	202,700	268,625	233,325	193,500	122,900
	1,000,000	568,500	501,950	661,000	594,450	447,000	313,900

*The above examples show that under the new Act estate tax, generally speaking, will be lower than under the old Act.

under 21 years of age, or otherwise dependent, survive, this exemption is increased to $60,000 with an additional $10,000 for each such child. Where no spouse survives, the exemption for each dependent child is $15,000. For example, where the net aggregate Estate amounts to $90,000, and a widow and two minor children survive, a total of $80,000 may be deducted from the taxable value of the Estate, leaving a net taxable Estate of $10,000.

An interesting aspect of the new Act is that the foregoing deductions may be taken whether or not the surviving widow or children actually benefit. Under the old Succession Duty Act, a widow is granted an exemption of $20,000, plus $5,000 for each dependent child, less the value of any benefit passing to any such child.

A net Estate under $50,000 is not taxed, either under the new or the old Act.

The Notch Provision

Under what is called the notch provision, a formula is provided that prevents the tax on Estates that are slightly in excess of $50,000 in value from being more than one-half of the excess over $50,000, and eliminates tax on Estates of less than $50,000. For example, in an Estate having a net value of $52,000, and assuming the minimum personal exemption of $40,000, the tax according to the table of rates in the Act would work out to $1,380, but by the application of the notch provision the tax payable would be reduced to $1,000, this being one-half the amount by which the net value of $52,000 exceeds $50,000.

As a further example, in an Estate having a net value of $51,000, and assuming the minimum personal exemption of $40,000, the tax according to the rates in the Act would work out to $1,240, but by the notch provision would be reduced to $500, or one-half the amount by which the net value of $51,000 exceeds $50,000.

The notch formula is not applied in Estates having a net value of more than $53,056. Above that figure the tax according to the rates in the Act does not work out to more than half the excess over $50,000 except in very large Estates, in which it is not the intention of the Act to reduce the tax. The new notch provision is different from that in the old Act, which merely provided that the duty could not be greater than the amount by which the Estate exceeded $50,000 in value.

Life Insurance

The new Act broadens the conditions under which the proceeds of insurance on the life of the deceased are subject to tax. Generally speaking, such proceeds are now taxable if the deceased owned or controlled the insurance policy, either alone or jointly with another person in the manner or degree set out in the Act, such as, for example, through a trustee under a trust controlled by the deceased, or through a corporation controlled by the deceased, where the whole or a part of the proceeds is payable to the spouse or child of the deceased, or for their benefit.

In certain circumstances insurance proceeds are taxable when payable to a corporation controlled by the deceased, but in this event the stock of the corporation is valued without taking the insurance into account.

PERSONS DOMICILED OUTSIDE CANADA

Tax Payable

The new Canada Estate Tax Act provides for tax at the rate of 15% on property situated in Canada belonging to persons domiciled outside Canada at the time of death, with a basic exemption of $5,000. In determining the value of the property for the purpose of this tax, no deduction may be made for debts other than those specifically made chargeable to the property.

The Notch Provision

The effect of the notch provision in Estates of persons domiciled outside Canada is that the tax liability cannot reduce the value of the Estate to less than $5,000.

Provincial Tax Credit

A credit is allowed in Estates of persons domiciled outside Canada in respect of duty paid to a Canadian Province. The credit comes to one-half the Federal tax applicable to the taxable property, provided the Provincial duty has been paid.

Situs of Property

The Act sets out fairly extensive rules for determining the situs of property in Estates of persons domiciled outside Canada. An important new rule is that bearer bonds issued by a Canadian corporation are deemed to be situated in Canada. Substantially, the rules are similar to those contained in the Succession Duty agreements between Canada and certain other countries.

This information is not presented as a comprehensive coverage of Estate Tax legislation. Our purpose is merely to draw attention to some of the important changes that will come into force with the new Canada Estate Tax Act, and we hope that in this sense it will be helpful.

No indication has yet been given as to the effective date of this legislation. Two dates have been mentioned —January 1, 1959 and April 1, 1959—but we understand that the Minister of Finance has, so far, refused to name a specific date.

MEDICAL MEETINGS

WORLD MEDICAL ASSEMBLY

The World Medical Association held its Twelfth General Assembly in Copenhagen, Denmark, August 15-20, 1958. This was preceded by the 33rd Session of the W.M.A. Council and followed by the 34th Session, August 21-22.

Council met in the Domus Medica, the headquarters of the host association, the Danish Medical Association, and the General Assembly convened in the Chamber of the Upper House of the Danish Parliament in the Christiansborg Palace, which lies in the centre of the city almost entirely surrounded by the salt-water canals.

For the first time, the World Medical Association, in conjunction with the American Medical Association and Johnson & Johnson International, held an International Medical Film Exhibition as part of the Assembly. Films were shown before morning and afternoon sessions each day, the sound being relayed in French, Spanish and English. Films, which were in some cases commented upon by their producers, came from the U.S.A., U.K., Denmark, Australia, Japan and Brazil and covered a wide range of subjects from otology to proctology. They were all of a high standard and were well received by an appreciative audience.

The usual Technical Exhibition with multilingual personnel available to demonstrate commercial products was opened officially by the newly installed President on Saturday, August 16.

The Assembly began on Friday, August 15, with a Medical Editors' Conference chaired by the Editor of the *British Medical Journal*, Dr. H. Clegg. The editors, who came from both sides of the Atlantic, discussed three aspects of the general topic "Medical publication as a responsibility of the medical associations". They first considered the coordination and integration of medical publications, leading papers being given by Prof. M. Fog, Editor of the official journal of the Danish Medical Association, *Ugeskrift for Laeger*, and Dr. J. R. Gosset, director of *Concours Médical* (France). They then considered the role of medical publications in postgraduate education, with papers by Dr. K. H. Backer, editor of the Danish journal of general practice, and Dr. E. Mazanek (Austria). Finally they discussed financial aspects of medical publication, discussion being led by Prof. P. Bonnevie (Denmark) and Dr. S. Gilder (Canada).

The scientific program of the Assembly was held on Sunday morning, August 17, with Prof. K. Brochner-Mortensen (Denmark) in the chair. Prof. Meulengracht (Denmark) described the Danish program for cancer control and eradication, outlining the extraordinarily effective statistical system in his country. Dr. Myschetzsky (Denmark) then read a paper on the therapeutic program in use at the poisoning control centre in Copenhagen, where centralization and uniformity of treatment has drastically reduced mortality from barbiturate poisoning, unfortunately a common occurrence in Denmark. Finally, it was a very heartening experience to hear a Dane (Dr. J. H. Thaysen) and a German (Prof. H. W. Bansi) discuss scientifically and objectively the permanent sequels of malnutrition as seen in concentration camp victims of World War II.

Plenary Sessions

Dr. A. Rasim Onat (Turkey), President of the World Medical Association, opened the plenary sessions of the Assembly with an interesting address that highlighted the accomplishments of the physicians of Copenhagen and the Danish Medical Association. Dr. Charles Jacobsen (Denmark) was elected and installed as President of the World Medical Association for 1958-1959. In his inaugural address, Dr. Jacobsen told the Assembly that the Danish Medical Association had been organized in 1857 in order "by mutual assistance to produce, develop and maintain conditions under which the medical calling best can develop".

He noted that:

"The most important task of every national medical association is to exert a decisive influence upon the solution of the problems concerned with the health of the community, both general and individual."

"A united medical association including the entire medical profession is essential in obtaining a decisive influence."

"Modern progress in medical science tends to divide the medical profession into interest or specialty groups; only a national medical association which includes all these groups has the authority to speak for the entire medical profession of a country."

"To achieve recognition and influence at the international level, the World Medical Association must apply the same principles of representation and unanimity of purpose necessary for successful action at the national level."

In conclusion, Dr. Jacobsen paid tribute to his predecessors and the leadership of those who had guided the World Medical Association since its organization in 1947 and proposed that the Association adopt as its motto the words of the founders of the Danish Medical Association:

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"To stand united, to persevere and to show moderation, therein must an association such as that of the medical profession seek its strength and therein lies the strength."

The General Assembly were then addressed by Mr. H. C. Hansen, the Prime Minister and Minister of Foreign Affairs; Mr. Julius Hansen, Mayor of the Copenhagen Hospital System; and Dr. Johannes Frandsen, Director General of the National Health Services of Denmark.

The keynote address was delivered by Dr. John Henderson (U.S.A.), Medical Director of Johnson & Johnson. His topic was "World Unity Challenges the Health Team".

The following medical associations were approved for membership in the World Medical Association: The Medical Syndicate of Uruguay; the Viet-Nam Medical Association.

Interassociation Relationships

The Council recommended and the General Assembly adopted the following policy on interassociation relationships:

"Without infringing on the rights of any member association, any communication from a member association intended for the government of the country of another member association should first be sent to the member association of that country for an opinion (with a copy to the Secretary General of the World Medical Association), and the opinion of that member association should be respected."

The annual report of Council to this General Assembly, presented by Dr. L. Garcia-Tornel (Spain), was given in two sections separated by a special address by Dr. Louis M. Orr (U.S.A.) on hazards of nuclear experiments. Dr. Orr gave figures to show that if nuclear weapon testing were continued for 30 years at the maximum rate so far attained, it would contribute only the negligible amount of 0.2 roentgen to the general radiation exposure of the population.

Reports of regional secretaries to the Assembly included references to the poor financial prospects for young physicians in India, Yugoslavia and Germany; the interesting changeover from a salaried physician system to a free-choice, capitation fee system by the leading social security agency in Israel, the welcome trend in Australia towards heeding the voice of organized medicine in government circles; and the new problems in Europe resulting from attempts to create a uniform social security system in the six countries forming the new European Economic Community. There has been a serious conflict between the medical profession and the government in Chile, where all but emergency medical activity ceased for four days as a protest against refusal of government to recognize the just claims of the profession.

Reports by various committees (W.M.A. Publications, *World Medical Journal,* Medical Education, Miscellaneous Business, etc.) were discussed. Preparations for the Second World Conference on Medical Education, to be held in Chicago, August 31-September 4, 1959, are well in hand. The proceedings of the conference will be edited by the American Medical Association. The Committee on Ethics has mainly been considering the ethical aspects of experiments on human beings, and of health education of the public through the mass media.

The Assembly adopted the report of the Planning and Finance Committee, presented by Dr. T. C. Routley (Canada), which recommended a radical revision in the financial structure and fee schedule of the World Medical Association, which will mean that from 1960, all W.M.A. funds will come to the Association directly from member associations, assessed on ability to pay.

An afternoon session on socio-medical affairs began with papers on health education of the public from Belgium, Britain and Japan, and a paper on mental hygiene and public health from Cuba. The report of the Committee on Medico-social Affairs summarized discussions organized by the World Health Organization on the role of hospitals. These revealed a concept unacceptable to W.M.A., namely the idea of the hospital rather than the family doctor as the focal point in medicine. W.M.A. is to investigate the world situation as regards the relation of hospitals to medical practice. It will also establish principles relating to contents and methods of health education.

At the Thirteenth World Medical Assembly in Montreal, the topic of medical economics will come in for special discussion.

At the present Assembly, the Canadian delegates were Dr. Léon Gérin-Lajoie, who was elected as President-Elect by acclamation, and Dr. Norman H. Gosse; alternates were Dr. A. D. Kelly and Dr. Margaret Gosse. Dr. S. Gilder was also present in his capacity as Associate Editor of the *World Medical Journal.*

The following were elected to office by the Twelfth General Assembly: Council, 1958-1961: Dr. Hugh Clegg (U.K.), Prof. Dr. L. A. Hulst (Netherlands), and Dr. Felix Worré (Luxembourg).

The following were elected to office by the Council at its 34th Session for the terms 1958-1959: Chairman of Council, Dr. L. R. Mallen (Australia); Vice Chairman, Prof. L. A. Hulst (Netherlands); Executive Editor, Dr. Austin Smith (U.S.A.); Associate Editor, Dr. S. Gilder (Canada).

At the 34th Council Session, the various committees organized for the year and elected their officers as follows: International Liaison – Dr. Jean Maystre (Switzerland); Medical Education–Dr. E. S. Hamilton (U.S.A.); Medical Ethics – Dr. Hugh Clegg (U.K.); Miscellaneous Business – Dr. Otto Rasmussen (Denmark); Planning and Finance – Dr. T. C. Routley (Canada); Socio-Medical Affairs – Dr. Felix Worré (Luxembourg), Chairman, Dr. Rolf Schloegell (Germany), Secretary.

Thirteenth General Assembly

The Thirteenth General Assembly of the World Medical Association is scheduled to follow immediately the Second World Conference on Medical Education. The time-table for these meetings is: Second World Conference on Medical Education – Chicago, Ill., August 30-September 4, 1959; Thirteenth General Assembly, the World Medical Association – Montreal, Que., September 7-12, 1959.

PUBLIC HEALTH

PREVENTION AND CONTROL OF STAPHYLOCOCCUS INFECTIONS IN HOSPITALS

The American Hospital Association has prepared a valuable bulletin on the prevention and control of staphylococcal infections in hospitals. After summing up current knowledge of the problem, the bulletin makes the following recommendations.

I. All hospitals should establish Committees on Infections, to devote particular attention to infections which are acquired in hospitals so they may be reduced to the lowest possible minimum.*

A. It is suggested that the Committee on Infections include, where possible, a bacteriologist, a pædiatrician, a surgeon, an internist, a nurse, and a hospital administrator. The local health officer should be urged to serve as a consultant to the committee. The committee should report periodically to the executive committee of the medical staff.

B. The functions of the Committee on Infections should include at least the following:

1. To establish a system of reporting infections among patients and personnel, such a system being essential to a proper understanding of infections which are acquired in hospitals. The committee should have access to all reports of infections anywhere in the hospital.
2. To keep records of infections as a basis for the study of their sources and for recommendations regarding remedial measures.
3. To distinguish to the best of its ability between infections acquired in the hospital and those acquired outside.
4. To review the hospital's bacteriological services to make sure that such services are of high quality and are accessible either in the hospital itself or in an outside laboratory. Bacteriophage typing, if not available in the hospital, may be sought, as needed, through official local and state health agencies.
5. To review aseptic techniques employed in operating rooms, delivery rooms, nurseries, and in the treatment of all patients with infections and, if indicated, to recommend methods to improve these techniques and their enforcement.
6. To make vigorous efforts to reduce to the minimum consistent with adequate patient care:
   (a) Use of antibiotics, especially as "prophylaxis" in clean, elective surgery.
   (b) Treatment with adrenocortical steroids.
7. To undertake an educational program to convince medical staff and hospital employees of the importance of reporting to responsible authorities when they have skin infections, boils, acute upper respiratory infections, and the like.
8. To establish techniques for discovering infections which do not become manifest until after discharge from the hospital, it being known that such infections are often overlooked because they may not be apparent until several weeks after the patient has left the hospital. Two approaches to discovering such infections are suggested:
   (a) An attempt to trace the source of any infection with which a patient may be admitted. For example, if an infant is admitted with staphylococcal pneumonia or a recently delivered mother with mastitis, the hospital where delivery occurred should be determined and informed of the infection so that it can seek possible sources of infection.
   (b) Periodic telephone polls on a random sample of discharged patients (particularly recently delivered mothers, newborns, and postoperative patients) to ascertain their state of health and, in case of any indication of infection, to follow them up. Such surveys have proved quite simple and quite valuable. A detailed account of the method is given by Ravenholt and others in the October 1956 issue of the *American Journal of Public Health*.

II. Hospital administration should undertake the following measures to assist in the control of infections:

A. Diligent maintenance of the general cleanliness of *all* areas in the hospital, not simply in those associated with operating rooms, delivery rooms, and nurseries. Other possible sources, such as dust, air pollution (special attention should be given to ventilating and air-conditioning systems and their filters), and floors must also be considered as potentially important factors in the spread of infection. There should be regular inspections of the hospital for general cleanliness.

B. Special studies among staff and personnel to uncover silent carriers of staphylococci, especially in epidemic situations accompanied by repeated cases traceable to the same organism.

C. Appropriate measures for the treatment of all carriers who persistently show heavy growth of epidemic strains of staphylococcus in nasopharyngeal cultures or who are identified by epidemiological evidence.

D. Transfer of such carriers and personnel with skin infections, boils, acute upper respiratory infections, and the like from locations such as operating rooms, delivery rooms, food-handling positions, and nurseries to other duty stations in the hospital. Usually such transfers have proved to be sufficient to control the problem, but occasionally leave of absence for a persistent carrier has been necessary.

III. Hospitals should initiate or participate in community programs to control infection through cooperation with other hospitals, local medical societies, local health departments, and other groups.

*The Joint Commission on Accreditation of Hospitals is being asked to consider the establishment of a Committee on Infections as a major factor in the accreditation of a hospital. Bulletin 17 of the Joint Commission contains recommendations on the subject.

EPIDEMIC OR UNUSUAL COMMUNICABLE DISEASES IN CANADA

During the week ending August 16, 1958, the Epidemiology Division of the Department of National Health and Welfare, Ottawa, received the following surveillance reports of epidemic or unusual communicable diseases.

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POLIOMYELITIS

MANITOBA—Dr. R. M. Creighton, Director of Preventive Medical Services, has reported five cases of poliomyelitis since August 1, bringing the provincial total to 15. Four cases have occurred in Greater Winnipeg and one in rural Manitoba. One of these is in a male, aged 64, with paralysis in both legs. None of the patients had received the vaccine.

RABIES (BATS)

BRITISH COLUMBIA—Dr. Stewart Murray reports one case of rabies in a bat in the Okanagan Valley. This makes three confirmed cases in the past 13 months, two in the Lower Mainland of B.C. and in the last instance, in the Interior. Two of the cases came under study as a result of bites in children. One child was given vaccine with no untoward reaction. The second child is receiving the vaccine.

EPIDEMIC DIARRHŒA OF THE NEWBORN

Vancouver, B.C.—A report has been received from Dr. Murray of 7 cases of epidemic diarrhœa of the newborn, due to pathogenic *E. coli*, having occurred in the past two weeks at a local hospital. The strain is 0119:B14. The organism is sensitive to neomycin and polymyxin. No new cases have been reported in the past six days. One death occurred. This was in a premature infant from whom the organism was isolated.

LETTERS TO THE EDITOR

THE EFFECT OF ATROPINE ON THE GALL-BLADDER

To the Editor:

For years it has been accepted that atropine and atropine-like compounds are indicated in the therapy of biliary colic. The rationale appears to be that atropine, through parasympathetic blockade, causes relaxation of smooth muscle.

The gall-bladder is under both nervous and hormonal control. The exact nature of the nervous control is debatable. Best and Taylor, in their textbook of physiology, seem to favour the view that vagal fibres are motor to the gall-bladder and inhibitor to the sphincter of Oddi. One might postulate, then, that a parasympathetic blockade with atropine would result in relaxation of the gall-bladder and possibly increased tonus of the sphincter of Oddi. Such an action would produce distension of the gall-bladder and possibly stasis of bile flow.

Recently, in our laboratory, we have necropsied 14 young dogs which were given a daily subcutaneous injection of 16 mg. per kg. body weight of atropine alkaloid dissolved in olive oil, for a period ranging from 7 to 21 days. This dose and vehicle were selected to ensure a maximum vagal blockade over a 24-hour period with only one daily injection. We were impressed with the grossly distended gall-bladders containing thick, greenish-black bile in the atropinized animals. The controls had normal-appearing gall-bladders with a slightly viscid amber-coloured bile. Most of the atropinized animals had reduced bile-staining of the duodenal contents. There was an increase in the volume of bile which averaged 490 ± 140% (mean ± standard error). There was marked thinning of the walls of the gall-bladders.

These findings support the view noted above concerning the effect of parasympathetic blockade on the gall-bladder.

It is our opinion that the use of atropine and atropine-like drugs in gall-bladder disease, although perhaps productive of symptomatic relief, should be scientifically reassessed because of the possibility of the production of bile stasis with distension and the complications thereof.

STANLEY V. JARZYOL, M.D. AND
DONALD W. MILLS, M.D.,
Research Associates.

Department of Pharmacology,
Queen's University,
Kingston, Ont.,
August 26, 1958.

LACRIMAL HYPOSECRETION

To the Editor:

In his very interesting paper on lacrimal hyposecretion (*Canad. M. A. J.*, 79: 371, 1958), Dr. Elliot mentions the congenital absence of tears in infants with corneal hypoasthesia, difficulty in swallowing, constant drooling, awkward gait, cyclic vomiting, and paroxysmal hypertension. Another condition discussed in that paper is keratoconjunctivitis sicca, or Sjögren's syndrome, a rare disease affecting mostly females over 40 years of age and presenting various symptoms and signs of a systemic disease. However, I missed a mention of "familial dysotonomia" or Riley-Day syndrome in which defective lacrimation (crying without tears) is one of the leading signs. This condition has been described by Riley *et al.*, in 1949, as a rare disease entity, interesting ophthalmologists, pædiatricians and neuropsychiatrists alike. The condition may be less rare than is generally assumed, but is likely not recognized as such, because knowledge of it does not seem to be widespread enough among physicians throughout the world. In 1954, I had an opportunity to observe a child suffering from this condition, coming to Vienna from its native country in South America (*Wien. med. Wchnschr.*, 105: 189, 1955). In 1955, I had the opportunity to observe another case in Brandon, Manitoba, in co-operation with Dr. William Forster (*J. Ment. Sc.*, 102: 345, 1956). According to Dr. C. M. Riley of Columbia University, whom I met at the New York Presbyterian Hospital in June 1957, a few cases of familial dysotonomia have been seen, although not published, in Canada.

Since it seems advisable to bring the existence of this syndrome to the attention of Canadian physicians, I would like to outline the main features of this interesting condition. In addition to the defective lacrimation which is present in all cases, the corneal reflexes are absent; the deep reflexes are often absent; there is a general hypoalgesia; symmetrical blotchy erythema following emotional disturbances or eating; excessive perspiration; sialorrhœa; emotional lability and poor motor co-ordination. Associate signs are: periodic vomiting, intermittent hypertension, unexplained bouts of pyrexia, proneness to acquiring respiratory diseases, orthopædic changes (scoliosis, pes cavus), epileptiform convulsions, and attacks of apnœa during the first year of life. The syndrome occurs in children of Jewish

parentage and is familial. The etiology is unknown and the pathology not well understood. Treatment so far has been disappointing and the prognosis cannot be assessed to any degree of likelihood, because of the relatively small number of cases reported and the comparatively short time which has elapsed since the syndrome was first made public. It is felt that widespread knowledge of this syndrome will provide opportunities for further clinical, laboratory and perhaps also pathological investigations.

459 Bloor St. W., M. TYNDEL, M.D., Ph.D.,
Toronto 4, Ontario,
September 5, 1958.

FATHERS AND SONS

To the Editor:

It is now 47 years since my five months' apprenticeship ended abruptly. It was on my first eclamptic case when my preceptor died! He was 58. All his family passed 80; three passed 90; one passed the century! He had practised in one place since 1880. A pupil of Osler, he went in the early nineties to get Lister's ideas first hand. His pulse had been about 30 for about two years. "When it gets to 26 I am very uncomfortable," he remarked one day as we were driving behind his spirited team.

He was not my father, but he became the grandfather of my three medical sons. Next month he will become the great-grandfather of a pre-medical student.

In this there has been no compulsion, no bursaries, no outstanding scholarship—ordinary workmen seeing the need and enjoying the privilege of rural medical life.

I came of farming stock. I learnt my first lessons in medicine in front of the kitchen stove, my mother vaccinating neighbouring children with scabs from other children's arms. (Only a bit later, points of bone with dried lymph were obtainable.) Shortly afterwards a wonder drug (Roux antidiphtheritic serum) worked a miracle on my playmate; he lived when so many others died.

Then there were the farm animals! The cow with the tuberculous shoulder; the piglets and lambs which seemed to refuse to live. The turkeys which preferred to die. They called for postmortems!

The sick neighbours—the woman with severe accidental burns, treated with chicken-manure dressings, dying soon after in childbirth. The village "ramancheuse" (bone setter) who treated sprains and breaks with white of egg and fresh eel-skins—the other woman who charmed away nose bleeds—the village shoemaker who made boots to fit his knees and walked on them because of polio—the great number of endemic goitres — the village hunchbacks. All this and much more within one league of a capital city—the *need* had to be filled.

Six years in a city studying, with summer farm work to keep the pot boiling, made me shake the dirt of the city from my feet. Some 40 hours after "capping" I assisted my preceptor with my first home delivery! There is still a need to fill.

Hardly a week goes by but some old crone—some old gaffer—says to one of us, "The old doctor never refused a call!" "The old doctor did better than that! The baby lived." "The old doctor didn't have the medicines you have, but . . . ." If Michael Brown, doctor's son and scholarship man, thinks this tradition is of slight value, he has another "think" coming! One hundred and five years of service to the same community seems to me worth while, worth perpetuating. To date not one of us regrets his calling.

I cannot understand the medical parent who does not shape his children's way of living to medicine or nursing for fear of that bogeyman, State Medicine. There'll always be a need to fill, always a job; depression or prosperity, there'll be a job to do if the seeker looks in the right place for it.

True enough, doctors' sons are not all saints. (Nor all sinners!) True, too, that many of our best practitioners have families with other backgrounds. But if the medical father is modern enough or unfortunate enough to have a downtown office "by appointment only!" or is a "two-month holiday man", it is natural his son will not be touched by his business more than the ordinary broker's son is touched by financial matters. Brokers' sons have been known to follow in their father's steps—why not doctors' sons? They'll both make good or bad practitioners according to their abilities.

If the doctor is lucky enough to be old-fashioned enough to be on call the year long, has his office in his home, and is wise enough to share his problems with his sons, a good proportion of them will follow in his steps — some of them may even be brilliant in spite of having a medical background!

Congratulations to Michael Brown for criticizing the editor! May he succeed in all he undertakes! He is at the beginning of a great adventure—the practice of medicine. He need not worry; there is no class danger in the practice of medicine properly handled in this country.

H. J. G. GEGGIE, M.D.
Wakefield, Quebec,
August 18, 1958.

THE ENTEROVIRAL EPIDEMICS

To the Editor:

We were interested to read the letter of Dr. Evans (*Canad. M. A. J.*, 79: 291, 1958) in which he contends that the clinical symptomatology of ECHO 9 infection observed by him was distinguishable from that of rubella. We do not disagree that the cases observed by Dr. Evans have justified his conclusion. In our own series of 66 cases, from which ECHO 9 virus was isolated from stools, throat washings and cerebrospinal fluids, there were instances when it was difficult to distinguish the condition from rubella. Unfortunately, ECHO 9 disease is only one of a large group of ECHO infections. Today, 26 different types of ECHO virus have been recognized. Thus, Horstmann,[1] in a reference to 20 types of ECHO virus, comments that types 4, 6, 9 and 16 are associated with rash in some cases. Furthermore she concludes that "The character and distribution of the eruption is similar to that of rubella and indeed sporadic cases without meningeal signs or cases occurring early in epidemic are frequently mistaken for rubella."

To complicate the present situation, exanthem has been observed with certain Coxsackie A9 infections together with infections associated with new strains

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not belonging to any of the 20 designated viruses. Another relevant point is that the eruption is commonly erythematous, maculopapular, and occasionally petechial, and a single virus type can produce any of the various types of eruption. In view of the evidence, we would hesitate to suggest that rubella can always be differentiated clinically from ECHO 9 virus or from ECHO viruses 4, 6 and 16, or Coxsackie A9 infection. Likewise certain others, the pathogenesis of which has not yet been established.

C. E. VAN ROOYEN, M.D.,
Department of Bacteriology, A. J. MACLEOD, M.D.
Dalhousie University, AND RUTH FAULKNER, M.Sc.
Halifax, N.S.,
August 28, 1958.

REFERENCE

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FUNCTIONING ISLET CELL TUMOURS IN DIABETES MELLITUS

To the Editor:

It is becoming increasingly apparent that the presence of an insulin-producing tumour in a patient with diabetes mellitus is not such a rare phenomenon as is sometimes stated. In the past two years five proven cases have been published.[1-5] The possibility of this combination of diseases should always be considered. The "syndrome" is represented in the typical patient by a long history of diabetes mellitus and the recent onset of recurrent attacks of hypoglycæmia. These patients usually require less insulin than formerly. The symptoms of hypoglycæmia are headache, chills, sweating, fever, restlessness, mental confusion, convulsions and coma in order of severity. The blood sugar may not be reliable as an indication of hypoglycæmia because of the modifying effect of the diabetes.

Surgical removal of the islet cell tumour will prevent the severe changes in the nervous system which occur owing to the spontaneous hypoglycæmia. Insulin injections for the diabetes mellitus tend to camouflage the real reason for the hypoglycæmic attacks. After the removal of the tumour from the pancreas, the patient still has diabetes but the insulin requirements are the same as before the tumour was present.

The mortality rate for the five reported cases[1-5] is 80%. One patient survived after surgical removal of the tumour but mental deterioration had already occurred as a result of the previous hypoglycæmic attacks.

In conclusion, it is to be hoped that with increased clinical awareness of this "syndrome" the results will be better in the future.

A. H. MERCER, M.D.
25325 Coolidge Highway,
Oak Park 37, Michigan, U.S.A.,
August 6, 1958.

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THE LONDON LETTER

(From our own correspondent)

GENERAL PRACTICE IN THE N.H.S.

Of the £585 million which the National Health Service cost in 1957, just under £63 million was spent on general practice, whilst the hospitals absorbed around £360 million. The drug bill was £54 million. These are some of the hard financial facts of life presented to the nation by the Minister of Health in his recently published annual report for 1957. His review shows that there are 19,343 principals and 465 assistants in general practice. Some of 67% of principals are in partnership, the vast majority of partnerships consisting of two doctors. There are 50 consisting of six doctors or more. There were 1331 practitioners aged 66 and over, 616 of whom were in single-handed practice. Among the assistants there were eight who were aged 76 or over. The average number of patients per doctor was 2273. Only 1763 general practitioners attended refresher courses during the year.

M.R.C. AND U.N.

With commendable promptitude the Medical Research Council has published its comments on the United Nations report on the effects of atomic radiation. Emphasis is laid upon the essential agreement between the United Nations report and the two previous ones—from the Medical Research Council and from the U.S. National Academy of Sciences. The major point on which the M.R.C. differs from the United Nations scientific committee is on the vexed question of whether or not there is a threshold dose concerned in the induction of leukæmia and cancer. In the view of the M.R.C. there are not yet sufficient data to justify any dogmatic statement on this point, whereas the United Nations committee tended to base their calculations and predictions on the fact that such a threshold exists. On the question of irradiation due to diagnostic radiology, the M.R.C. point out that in their 1956 report they put this contribution at around 22% of the natural background radiation. They now say that further information indicates that the genetically significant dose from this source may be as much as 100% of the natural background radiation in countries with extensive medical facilities. Needless to say, this particular aspect of the subject is the one which has received most publicity, but the M.R.C. takes comfort in the thought that most of the genetically significant dose comes from a few types of radiological examination.

CHILDREN IN HOSPITAL

Children's hospitals have been much to the fore of recent weeks in both the medical and the lay press. Yet another maladroit move on the part of the authorities was responsible for what developed into a somewhat embittered controversy, but from the long-term point of view probably nothing but good will come out of it. The spark which set things off was a threatened move on the part of the South West Metropolitan Regional Hospital Board to close Queen Mary's Hospital for Children, Carshalton, Surrey, which is the largest children's hospital in the south of England. This, of course, was a complete reversal of recent trends to remove children from adult hospitals and concentrate them in special hospitals where they

would be able to receive the expert medical, surgical and nursing attention which is now recognized to be essential for efficient pædiatric treatment at the present day. In view of the publicity given to the subject it is highly improbable that the Ministry will now close down this particular hospital. What is much more important, however, is that the whole subject has been adequately aired, and intelligent laymen, as well as the medical profession, have been able to judge for themselves exactly the advantages to be gained from restricting the care of children to specialized hospitals. One of the significant factors brought out has been the demonstration of the recent tendency to utilize the old fever hospitals, for which there are now so few demands for their original purpose, as children's hospitals. Equally valuable has been the attention drawn to a point which has tended to be ignored recently—the advantage of having a certain number of hospital beds available in rural areas for the treatment of children who are too ill to be nursed at home but who do not require anything like specialized treatment.

"Retreats" for Smokers

Earlier this year reference was made in this correspondence to the setting up by the National Society for Non-Smoking of smokers' clinics. These have proved so successful that the Society is now planning to organize weekend courses for tobacco addicts. The first of these is to be held this month in a guest house on the Isle of Wight. There are places for 65 "students" at £3 each. Lectures will be given by a panel of specialists, including chest physicians, psychotherapists and medical officers of health. Lest the "no smoking" ban, which will be imposed, proves too much for those attending, the possibility is being considered of having a hypnotist in attendance to assist the weaker brethren. One cannot but admire the missionary zeal of the members of this society in their valiant attempts to rescue tobacco addicts from the hazards so vehemently stressed by the statisticians.

London, September 1958. William A. R. Thomson

ABSTRACTS *from current literature*

MEDICINE

Unilateral pulmonary Artery Absence or Hypoplasia.
J. C. Elder *et al.*: *Circulation*, 17: 557, 1958.

Five cases of unilateral absence or hypoplasia of a main branch of the pulmonary artery are described. This is the largest series in which the diagnosis has been made before autopsy or surgical exploration. The radiologic findings are thoracic asymmetry and disparity between the vascular markings in the lung fields. The resting pulmonary artery pressures are usually normal, but on exercise there is an exaggerated rise in pulmonary artery pressure. With occlusion of a segment of the existing pulmonary vascular system by a balloon-tipped catheter there is a marked rise in pulmonary artery pressure. There is negligible oxygen uptake on the side of the absent artery. The condition is emphasized as a clinical entity which usually causes symptoms. S. J. Shane

Cardiovascular Hæmodynamic Functions in Complete Heart Block and the Effect of Isopropylnorepinephrine.
M. F. Stack *et al.*: *Circulation*, 17: 526, 1958.

In four elderly subjects with complete heart block and without clinical evidence of congestive heart failure there were noted elevated pressures in the right heart, increased systolic and pulse pressure in systemic arteries, increased systemic and pulmonic vascular resistances, reduced cardiac output in spite of increased stroke volume, increased A-V oxygen difference and impaired renal hæmodynamic functions.

In one younger (39 years) subject with heart block the changes in systemic and cardiac pressures were the same as in the elderly subjects, but stroke volume was increased sufficiently to compensate for the slow heart rate and cardiac output was normal.

The administration of isopropylnorepinephrine by intravenous injection, intravenous infusion, and sublingual tablet was associated with *little change in systemic or cardiac vascular pressures*, but with an increase in cardiac rate and cardiac output and a reduction in A-V oxygen difference in four of five subjects. The normal hæmodynamic status appeared to be due to both an increase in heart rate and a direct effect on heart muscle, each to varying degrees in the different subjects. S. J. Shane

Reliability of Subjective Circulation Time Determinations: Comparison of Objective and Subjective Methods.
M. M. Manl and K. Lange: *Circulation*, 17: 922, 1958.

In 100 patients, a comparison study of the circulation time determined with Decholin and the dermofluorograph revealed a 42.5% error in the Decholin method.

In 34 patients, a comparison study of the saccharin and dermofluorographic circulation times showed that the saccharin time was even less reliable than the Decholin time, with an even 56% error.

Decholin and saccharin circulation times appear to be highly unreliable, especially in patients in congestive heart failure, probably because the large residual cardiac volumes tend to increase the error.

Accuracy of the dermofluorographic method lies within ±5%, and circulation time with this instrument may be measured on unconscious patients, infants and children, and patients with language difficulties.
S. J. Shane

Therapy of Transverse Myelitis Occurring during Tuberculous Meningitis.
P. Chortis: *Dis. Chest*, 33: 506, 1958.

In a considerable number of cases of tuberculous meningitis, transverse myelitis may occur and localization of bacilli in the medulla spinalis is primarily due to direct extension. The myelitis appears in cases of prolonged and incomplete therapy of tuberculous meningitis and mainly when intraspinal injections of streptomycin have been administered for a long time. A preparation described as sulfone J.51 is stated to have a considerable therapeutic effect on meningomyelitis, especially when administered before complete degeneration and necrosis of a spinal segment. The histologic changes of myelitis consist of degenerative and necrotic changes of white and grey matter, accompanied by development of tubercles as well as extensive changes in the subarachnoid cavity vessels.
S. J. Shane

Systolic Murmurs.

A. LEATHAM: *Circulation*, 17: 601, 1958.

Graphic registration of heart sounds and murmurs (phonocardiography) has greatly facilitated analysis of their pattern, timing, and relation to hæmodynamics.

Systolic murmurs fall into two main groups—ejection murmurs and regurgitant murmurs—according to their shape and relation to the heart sounds.

Ejection systolic murmurs are separated from the first heart sound by the isometric contraction time; they are crescendo-diminuendo in pattern (diamond-shaped) and finish appreciably before the second heart sound. They are due to ejection of blood from the left or right ventricle into the aorta or pulmonary artery when there is stenosis of the appropriate valve or outflow tract, valve disease without stenosis, or without valve disease—increased forward stroke flow or dilatation of the aorta or pulmonary artery. Small ejection vibrations can be recorded in normal subjects and their physiologic accentuation is probably responsible for most systolic murmurs proved innocent.

Regurgitant systolic murmurs start with the first heart sound and finish with the second; the volume of sound emitted is relatively constant throughout systole or increased in late systole. They are caused by back-flow of blood through the mitral or tricuspid valve or by a left-to-right shunt of high velocity through a ventricular septal defect or patent ductus arteriosus.

S. J. SHANE

Bone and Joint Changes in Hæmophiliacs.

G. STIRIS: *Acta radiologica*, 49: 269, 1958.

The author describes the bone changes in hæmophiliacs, noting that there are three stages, viz. the hæmarthrotic, the panarthritic, and the regressive.

Swelling of the joints, with pain and reduced motility, is a prominent feature of the hæmarthrotic stage. Changes in the synovial membranes, joint capsules, cartilages and juxta-articular areas of bone, occur in the panarthritic stage. The regressive stage consists of increasing deformity of the joints and rigidity associated with the development of contractures.

The youngest patient was three and the oldest 11 years of age. The knee-joint was the most commonly affected, then the elbow and ankle in that order. Less frequently hæmorrhage was observed in the wrist and rarely in the shoulder, hip, finger and toe joints. The most characteristic findings were erosion and cyst formation. The cysts occur in the majority of the joints and vary in size, and are situated in the epiphyseal area chiefly, but do occur in the metaphysis and diaphysis.

The author reports material on 35 hæmophiliacs. Some excellent radiographs are included.

CHARLES E. VAUGHAN

Detection and Estimation of Aortic Regurgitant Flow in Man.

E. BRAUNWALD AND A. G. MORROW: *Circulation*, 17: 505, 1958.

A method for the detection and estimation of the magnitude of aortic regurgitant flow in man is described. Aortic regurgitant flow was detected by the injection of indicator dye at various levels in the descending aorta through a catheter introduced percutaneously from the femoral artery. The lowest point in the descending aorta from which injected dye regurgitated back to the ascending aorta and perfused the right ear was determined by means of an oximeter placed on the right ear.

In all seven patients without aortic regurgitation, dye injected distal to the aortic arch could not be detected in the right ear. In all 10 patients with clinical and hæmodynamic evidence of aortic regurgitation, dye injected into the descending aorta regurgitated to the ascending aorta. The technique was also found useful in demonstrating aortic insufficiency in patients with diastolic murmurs at the base of the heart, but without other hæmodynamic evidence of aortic valve disease.

Employing aortic pressure - volume relationships obtained from human cadavers the magnitude of aortic regurgitant flow was estimated. In 10 patients with aortic insufficiency the estimated regurgitant flow ranged from 1.2 to 2.8 litres per minute per square metre of body surface area.

S. J. SHANE

SURGERY

Aneurysm of the Abdominal Aorta.

T. H. SELLORS: *Brit. J. Surg.*, 45: 457, 1958.

Arterial grafting has rendered other treatments of aneurysm obsolete. The first successful graft to replace an aneurysm of the abdominal aorta is attributed to Dubost, Allary and Oeconomos in 1951. Now the operation has a mortality rate of less than 20%. The average life of a patient with abdominal aneurysm is two years from the time of diagnosis, though there are records of patients living as long as eight years without treatment. Aneurysm of the abdominal aorta tends to be fusiform rather than saccular. Occlusion by thrombosis usually occurs below, in the iliac arteries. Aneurysms rarely develop above the level of the renal arteries, the dilatation usually beginning a centimetre or so below them. Collaterals from the superior mesenteric artery often extend to supply the lower colon. Dissecting aneurysms usually begin in the thoracic aorta. Abdominal aneurysms are symptomless until they are on the point of rupture. This pain is ill-defined and hard to control. Surgical treatment should not be delayed once the diagnosis is made. Aortography is used to define the lesion.

The technique of the operation is discussed and two case reports are detailed.

BURNS PLEWES

Constrictive Papillitis with Biliary Obstruction.

S. L. WARD: *Western J. Surg. Obst. & Gynec.*, 66: 94, 1958.

Four cases of obstructive jaundice due to constriction of the duodenal papilla restricting the terminal opening of the common bile duct to the size of a pin-point are described. The literature and anatomy involved are reviewed. Most such cases are diagnosed as stone in the common bile duct. Jaundice may be slight or absent, depending on the degree of stenosis, but pain, nausea, anorexia and loss of weight are common. Previous instrumentation of the common duct is considered a significant factor. Intravenous cholangiography is important in making the diagnosis. Pancreatitis may complicate the case.

If dilatation of the sphincter of Oddi is not easy, sphincterotomy should be performed through an incision in the duodenum.

BURNS PLEWES

Prescalene Lymph Node Biopsy.

B. N. JOSEPHS AND F. M. WOODS: *A.M.A. Arch. Surg.*, 76: 93, 1958.

A review of all the prescalene node biopsies done in a Veterans Hospital in Boston for the diagnosis of an undiagnosed intrathoracic lesion showed 46 out of 125 cases to be positive. Comparison of the final diagnosis with the biopsy results showed 32 positive biopsies in 78 carcinomas of the lung, 7 out of 7 in Hodgkin's disease, 3 out of 3 in sarcoid, 2 out of 2 in carcinoma of œsophagus, and so on.

The value of scalene node biopsy is emphasized, for the operation is simple and is just about as good as a biopsy of mediastinal lymph nodes; it is free of serious complications. It provides a diagnosis in a significant proportion of cases even when the supraclavicular nodes are not palpable. In suspected bronchogenic carcinoma the biopsy result is often a determination of incurability.

The operation is done on the left side for upper lobe left-sided lesions; otherwise the right side is chosen. BURNS PLEWES

Transplantation of the Partially Resected Middle Œsophagus with a Jejunal Graft.

S. KATSURA, Y. ISHIKAWA AND G. OKAYAMA: *Ann. Surg.*, 147: 146, 1958.

The replacement of the resected œsophagus by a segment of upper jejunum was undertaken at Tohoku University because of the numerous postoperative difficulties encountered after œsophagogastrostomy: loss of appetite, burning sensations, fullness, reflux of food, and dysphagia. The intestinal continuity is restored by end-to-end anastomosis. Separate thoracotomy and midline laparotomy incisions are used.

It is stated that this operation is better because unnecessary removal of œsophagus and stomach is avoided. Lymph node involvement in carcinoma cases is very common, and this operation is not used when there is evidence of extension or metastases. There are difficulties in attempting to bring a jejunal loop into the neck, when a skin tube must often be used and in some cases short arterial arcades make a free jejunal graft impossible. The technique of discarding excessive caudal end of the graft seems to eliminate necrosis of the transplanted jejunum. Preservation of the gastric fundus lessens the fear of peptic ulceration. The difficulty of anastomosing colon to the œsophagus makes a jejunal transplant preferable. BURNS PLEWES

An Evaluation of Stripping Versus Ligation for Varicose Veins.

K. A. LOFGREN, A. P. RIBISI AND T. T. MYERS: *A.M.A. Arch. Surg.*, 76: 310, 1958.

As in other centres, the treatment of varicose veins has changed at the Mayo Clinic over the years. Before 1927, direct dissection and extraluminal stripping was done. From 1927 to 1937, injection therapy alone replaced operations. Then high ligation and retrograde injection was used till complete stripping was started in 1947. The operation done during the past ten years involved complete stripping of the main saphenous vein from the dorsum of the foot to the saphenofemoral junction, direct dissection of all superficial plexuses and tortuous veins, individual ligation and resection of all perforating veins.

Follow-up five years after operation showed a tremendous advantage for the stripping procedure, for 36% of the high ligation and injection series required further surgical treatment as compared with none in the later group. Results in the high ligation group showed 40% good and 5% fair results, while in the stripping group the results were 94% good and 6% fair. BURNS PLEWES

Congenital Dislocation of the Hip: Its Early Recognition and Treatment.

SIR HARRY PLATT: *Brit. J. Surg.*, 45: 438, 1958.

The early recognition and treatment of congenital dislocation of the hip was advocated first by Putti and depends on the observation of the clinical signs: shortened limb, tendency to eversion and limited abduction as noticed by the mother, and asymmetry of the skin creases, deepening of the inguinal sulcus, telescoping, and a click on full abduction to be found by the clinician. In bilateral dislocation, the lateral bulging of the trochanteric regions and the limited abduction in both hips are significant. The radiograph offers final proof. Spontaneous reduction is rare.

Treatment in infants by Putti's divaricator splint has stood the test of time. Though many practise treatment on an outpatient basis, hospitalization is favoured. In the author's series of 587 patients (743 dislocations), 35 patients were treated before the walking stage, and 25 of these were successfully handled by the divaricator alone. Five required manipulative reduction and another five went on to open reduction.

Less than 10% of hip dislocations are diagnosed before the child walks, and the physical signs are not always significant. In countries like Northern Italy where congenital dislocation is very common, the policy of encouraging mothers to bring their infants for inspection is warranted. Where the lesion is uncommon, mothers who have had the dislocation themselves should have their infants examined before the age of six months. Till early diagnosis is common, orthopædic surgeons will have to continue to perfect techniques of closed and open reduction. BURNS PLEWES

Fracture of the Os Calcis.

W. R. N. LINDSAY AND F. P. DEWAR: *Am. J. Surg.*, 95: 555, 1958.

This is a comprehensive review, sponsored by the Workmen's Compensation Board of Ontario, of a long-term follow-up of 174 patients with fractured calcanei. A total of 397 case histories of old fractures of the os calcis were examined and 30% showed no involvement of the subastragaloid joint. It involved a 5000-mile trip throughout the province for one of the authors to personally examine and assess the current condition of the foot in order to establish the cause of residual disability. The results in these injuries are generally poor and it would seem that too little attention has been given to the etiological factors underlying the symptoms which result in permanent disability.

The various classifications and mechanisms involved are considered, but it was not possible to classify the x-rays in this series in a detailed manner. Moreover, there did not seem to be much value in doing so, once damage to the subastragaloid joint was demonstrated. Instead three groups, namely (a) moderate degree of deformity, (b) severe degree of deformity, and (c) fractures involving the subastragaloid joint without displacement, are distinguished.

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At the ten-year follow-up, some patients claimed that they were still experiencing slow improvement in their foot, and cited activities they could do which they could not tolerate two years previously.

Patients may have a flare-up of rather severe pain lasting from a few days to three or four months with final return to their former state. In some it involved the heel or ankle, and in others the entire foot or even the leg. Pain and œdema do subside and are not an indication for subastragaloid arthrodesis, as is often recommended.

The end results were assessed on (a) the ability to perform heavy work, (b) the patient's ability to walk a mile and (c) the effect of the injury on the patient's life—i.e. the magnitude of constant symptoms. All patients who failed in at least two of the above factors were considered to have a poor result. A good result did not indicate that the patient was symptom-free, as only 27 patients (17%) had no complaints. It became apparent that the greatest percentage of good functional results lay in the conservatively treated groups.

The most serious complaint is pain, and because little attention has been given to its nature there has been a tendency to group the various types together. Several distinct types became obvious, but that located below the lateral malleolus was the commonest. It has commonly been said that this pain is due to damage to and interference with the subastragaloid joint. However in this series 36% of the patients with solid arthrodesis of the subastragaloid joint produced by early operation continued to complain of pain below the lateral malleolus. Lateral malleolar pain does not correlate with impingement of the lateral malleolar tip against the talus or against lateral thickening of the os calcis. The authors think that this type of pain is usually related to the lateral ligaments of the ankle joint.

Heel pain was quite common and the majority with this type had a marked deformity with reversed calcaneal angle or else a prominent and usually palpable bony exostosis of the bottom or side of the tuberosity.

After studying patients without pain it was felt that these good results do not tend to fall into any one treatment group. The pain may disappear even without severe deformity of the os calcis and with subastragaloid joint involvement. It is not felt that radiographic evidence of subastragaloid arthritis is an indication for arthrodesis as it is not necessarily associated with subastragaloid pain and may be absent when the pain is a prominent symptom.

The authors think that closed reduction of fracture of the os calcis is of doubtful value, and point out the 11% incidence of osteitis after insertion of wires or Steinmann pins. Although reduction may be indicated in fractures with severe deformity and not too much comminution, such attempts in this series were generally unsuccessful and did not increase the percentage of good clinical results.

Although results of immediate arthrodesis may not seem very good in this series, 60% obtained a good clinical result with early fusion. However, 76% of a similar series treated conservatively had a good outcome. Late subastragaloid arthrodesis is probably indicated in the treatment of some fractures of the os calcis with persistent "subastragaloid" pain. It is not indicated for lateral malleolar pain, heel pain, or ankle pain. Pain suggestive of origin in the subastragaloid joint as indicated by inversion and eversion tests must be carefully distinguished from pain originating in the ankle, as this is a likely source of error. Damage may occur here to the articular cartilages at the time of the injury or increased stress on the ankle may cause degenerative changes. In some cases arthrodesis was performed for subastragaloid pain, and postoperatively the same pain was present and appeared to come from the ankle. Radiological osteoarthritis of the subastragaloid joint is not an indication for fusion.

It is pointed out that some authorities condemn subastragaloid arthrodesis in favour of triple arthrodesis because the subtaloid and mid-tarsal joints function as one unit and simple subastragaloid arthrodesis failed to yield satisfactory feet in at least one-third of the fresh and one-half of the late lesions. One series (Conn) of 26 old cases is referred to, all with pronation of the heels, planus of the long arches, and valgus of the forefeet with persistent disabling pain, while 25 new patients treated with triple arthrodesis had good to excellent results in all but three instances.

Although the series of cases treated with tensor bandages alone is not large enough for definite conclusions, a review would suggest that little or no immobilization results in less stiffness. Tampering with the fracture or fusing the joints of the foot gives a greater number of poor results than does conservative treatment.

Attempts at reduction of the fracture displacement did not increase the percentage of good results in this series. Only 33% showed radiological evidence of improved position of the fragments. A failure to obtain perfect reduction did not alter the prognosis. Because of the complications of operative therapy and the questionable advantages of fusion, careful consideration should be given before fusion is contemplated. Moreover, arthrodesis is only rarely indicated in failure of conservative therapy. ALLAN M. DAVIDSON

Maximal Reconstitution of the Stenotic Mitral Valve by Neostrophingic Mobilization (Rehinging of the Septal Leaflet).

C. P. BAILEY AND T. HIROSE: *J. Thoracic Surg.*, 35: 559, 1958.

The senior author writes from a nine-year clinical experience including more than 2000 patients subjected to mitral commissurotomy through the standard left-sided approach, and close to 500 operated on during the past four years by the right-sided method. A new and technically much superior type of valve mobilization is described, based upon the principle of converting the irretrievably destroyed flutter-valve action of the mitral valve to an efficient flap-valve mechanism. This effect is accomplished by a rehinging or new hinging of the septal cusp, not only through its flexible mid-zonal tissue, but also with respect to the usually shortened papillary suspension yoke which must be split longitudinally. Such a maximally corrective procedure cannot, according to this author, be accomplished except with the technical advantage of the right-sided approach. The writers believe that most patients with mitral stenosis have obtained partial and often temporary relief of their valvular obstruction when the older left-sided commissurotomy procedure has been carried out. Restenosis ultimately may be expected in a proportion of these patients who have, in actuality, been subjected merely to linear and limited division of a fibrous stricture.

The writers believe that recurrence of mitral stenosis after their procedure will be rare, since the operation amounts to construction of a valve mechanism of different type, and since all the tissue cleavages extend well into normal unfibrosed structures.

The early operative mortality and morbidity associated with complete reconstitution of the valve are distinctly less than with less complete operations.

S. J. SHANE

GYNÆCOLOGY AND OBSTETRICS

Current Status of the Pregnant Cardiac.

J. M. KAUFMAN AND P. E. RUBLE: *Ann. Int. Med.*, 48: 1157, 1958.

Most hæmodynamic changes of pregnancy become significant early in the second trimester, and may greatly modify heart murmurs and other physical findings. Patients with either rheumatic or congenital heart disease should be evaluated both medically and surgically early in pregnancy. When cardiac symptoms appear early and surgical treatment is possible, surgery is preferable to abortion. In this study, 96 patients who had had mitral commissurotomy subsequently became pregnant, with only one maternal and one fetal death. Ninety-three mitral commissurotomies were performed during pregnancy, with three early cases of maternal mortality, probably avoidable with present anæsthesia and surgery. Eighty-eight live babies were delivered in this group. Twenty-two patent ducti were sectioned during pregnancy, with no maternal mortality and only one miscarriage one month after operation. Their results indicate that patients with various other types of congenital heart disease, such as coarctation of the aorta, tetralogy of Fallot, and interatrial and interventricular septal defects, may go through pregnancy safely. Though ideally performed before pregnancy, cardiac surgery is often a safe procedure for mother and baby during pregnancy. Heart surgery should be considered an adjunct to good medical management, and the patient should have the obvious advantage of careful medical management through pregnancy, delivery and the postpartum period.

S. J. SHANE

The Use of Urinary Sediment as an Aid to Endocrinological Disorders in the Female.

C. SOLOMON, P. PANAGOTOPOULOS AND A. OPPENHEIM: *Am. J. Obst. & Gynec.*, 76: 56, 1958.

The epithelium of the vagina, urethra and trigone is derived from the urogenital sinus. Exfoliated cells from these areas are similar in appearance and change with hormone stimulation.

Examination of the urinary sediment is valuable in young girls in whom vaginal examination may be believed to be too traumatic psychologically. It is also of value in cases of hæmorrhage which would obscure the vaginal cytology or when repeated examinations are necessary.

The authors have become particularly interested in the urinary sediment of pregnant women. If, as seems to be the case, a smear showing more than 30% of abnormal cells indicates that miscarriage is probable, perhaps obstetricians should add this examination to the prenatal list.

Urinary cytology studies are important in cases of senile urethritis as a measure of prognosis and therapy.

ROSS MITCHELL

THERAPEUTICS

Radioactive Phosphorus in Therapy of Leukæmia, Polycythæmia Vera and Lymphomas.

R. B. CHODOS AND J. F. ROSS: *Ann. Int. Med.*, 48: 956, 1958.

In this 10-year study, radioactive phosphorus was found to be an effective agent in the management of chronic granulocytic leukæmia, chronic lymphocytic leukæmia and polycythæmia vera. It was not of any significant benefit in Hodgkin's disease, multiple myeloma, acute leukæmia or mycosis fungoides. Its advantages include ease of administration, the infrequency of radiation sickness, and the fact that it can be given with minimal inconvenience to the patient.

The program of therapy used for each condition is presented. Treatment in leukæmia was individualized. Dosage was dependent upon the type of leukæmia, its current status and the response of the patient. Supplementary therapy with x-ray was used if needed to reduce splenomegaly or lymphadenopathy. Supportive therapy with blood, antibiotics and steroids was used as required. Radiophosphorus treatment of polycythæmia vera was also individualized. Initial or supplementary venesection, x-ray therapy or other treatment may be required in individual cases.

Leukopenia, thrombocytopenia and perhaps acute blastic leukæmia occasionally occurred after P^{32} treatment of the chronic leukæmias, particularly the granulocytic forms. Terminal leukæmia was also observed in polycythæmia vera, but the incidence probably did not exceed that encountered in polycythæmia vera treated by other methods.

S. J. SHANE

Treatment of the Dumping Syndrome.

G. L. JORDAN, JR.: *J. A. M. A.*, 167: 1062, 1958.

This study was undertaken to assess the results obtained in treating patients with the dumping syndrome. Of 400 patients who underwent gastrectomy for a variety of conditions (75% duodenal ulcer, 15% gastric ulcer), symptoms typical of this syndrome were experienced by 144 (36%). Almost all of them were followed up for periods of six months to four years or longer after the onset of symptoms. Of the 71 patients with mild symptoms, about half did not desire any treatment and the other half managed well on a restricted diet and with postprandial recumbency, only two patients requiring in addition an antispasmodic. Of the 64 who had moderate symptoms, eight patients preferred to put up with their symptoms rather than subject themselves to a regimen, one patient obtained satisfactory relief by diet and recumbency, and almost half the patients required antispasmodics. Four patients failed to obtain relief by any of the therapeutic regimens, but of them one patient had a spontaneous remission of symptoms after two years. None of the nine patients with severe symptoms could be managed by diet and recumbency alone. Two obtained complete relief and one had partial relief when antispasmodics were given in addition. The remaining five patients failed to respond to treatment but one of them subsequently had spontaneous regression of symptoms. The author found that once the use of an antispasmodic has been found necessary, it has to be continued indefinitely.

W. GROBIN

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Clinical Results with Methocarbamol, A New Interneuronal Blocking Agent.

H. W. PARK: *J. A. M. A.*, 167: 168, 1958.

Methocarbamol was evaluated in 42 patients with a variety of disorders manifesting an increase in involuntary muscle tone. In 30 patients with pyramidal tract and acute myalgic disorders, use of this drug resulted in a significant improvement in 27 (90%), questionable improvement in two, and none in one. There was no change in 12 patients with chronic arthritic, extrapyramidal, and myalgic disorders, as a result of drug administration. In all but two patients the side effects were reversed on slight reduction of dosage. No side effects developed after 72 hours on the medication. Methocarbamol has a sufficiently prolonged action to improve significantly the functional capabilities of patients with pyramidal tract disease. Results of these trials warrant further study of this type of medication. S. J. SHANE

Studies of Hepatic Function in Patients Receiving Promazine.

R. J. KORN *et al.*: *Am. J. M. Sc.*, 235: 431, 1958.

Promazine differs from chlorpromazine only in the absence of the chlorine atom from the carbon 2 position of the phenothiazine nucleus. Only one patient has been reported, thus far, to have developed jaundice during the administration of promazine. This patient had also previously received chlorpromazine. In the present study a large number of patients receiving promazine were carefully observed for the development of jaundice. In one-half of this group, the effect of the drug on the liver was studied by serial determinations of hepatic function. No evidence of jaundice or hepatic damage developed in patients receiving this drug.

Jaundice did not develop in any of 201 patients treated with promazine. Hepatic function was evaluated in 82 of these patients before and after promazine. Hepatic function remained normal in 44 and improved in 33 of the 38 previously abnormal. In no patients receiving promazine was there worsening of function. S. J. SHANE

Hinconstarch in Treatment of Pulmonary Tuberculosis.

V. C. BARRY *et al.*: *Am. Rev. Tuberc.*, 77: 952, 1958.

In this study, 52 patients with pulmonary tuberculosis due to isoniazid-susceptible tubercle bacilli were treated with hinconstarch for three to 12 months. Moderate or marked roentgenographic improvement was observed in 65% of patients at three months and in 80% at six months, with increasing percentages at longer intervals. Closure of all cavities was achieved without surgery in 55% of patients during the period of the trial. Disappearance of tubercle bacilli from the sputum occurred in 85% of the 52 patients.

A daily dosage of 40 to 45 mg. per kg. appeared to be an effective dose of hinconstarch which did not cause toxic symptoms. Doses substantially larger than this resulted in gastro-intestinal or renal toxicity.

In 2 of 10 patients (9 of whom had had extensive chemotherapy previously) whose bacilli showed a varying degree of isoniazid resistance, bacteriologic "conversion" was observed.

Hinconstarch is a polymer from periodate oxidized potato starch by condensation with equimolar proportions of isoniazid and p-aminobenzalthiosemicarbazone. S. J. SHANE

Streptovaricin: Therapeutic Effect on Guinea Pigs Infected with Tubercle Bacilli Resistant to Streptomycin and to Para-aminosalicylic Acid.

A. G. KARLSON: *Proc. Staff Meet. Mayo Clin.*, 33: 193, 1958.

Twenty guinea pigs were infected with tubercle bacilli resistant to streptomycin and to PAS. Four animals killed in 25 days were found to have visible tuberculous lesions. Treatment of eight of the remaining animals was started with 25 mg. of streptovaricin given orally once daily and was continued for 58 days. The other eight were used as controls. At the end of this period, 83 days of infection, only two of the controls were living and both showed loss in weight. Of the treated animals, six were living and apparently normal. All survivors were killed on the 83rd day of infection. All the control animals had extensive tuberculous lesions, but the treated animals presented little gross or microscopic evidence of active disease. The administration of streptovaricin, a complex antibiotic derived from *Streptomyces spectabilis*, caused regression and healing of tuberculous lesions that had been progressing when treatment was started. Further investigation is indicated. S. J. SHANE

Cellular Therapy *(in German)*.

J. BOSCH: *Wien. klin. Wchnschr.*, 70: 76, 1958.

The author describes his method of implantation of placenta tissue subcutaneously as originally proposed by Filatov. He carried out 2840 implantations over a period of eight years and reports the results in osteoarthritis of the knee, the hip and the spine and in a small number of rheumatoid arthritis cases as well as some with osteoporosis and ill-defined painful conditions. Generally speaking, 50% of the patients benefited from this treatment to a considerable degree, relief of pain occurring within a few weeks of the implantation and lasting as long as one year or more. Bosch takes issue with Niehans, whom he quotes as demonstrating some remarkable cures with his "cellular therapy". The cost of Niehans' injections is out of reach for the majority of patients. The claims put forward by Niehans are questioned by the author. The author's method is by contrast stated to be cheap, effective and as far as can be ascertained after eight years free of serious side effects. W. GROBIN

Radioiodine Treatment of Paroxysmal Supraventricular Tachycardia in the Euthyroid Patient.

E. CORDAY, H. GOLD AND H. L. JAFFE: *Circulation*, 17: 900, 1958.

Twenty-five euthyroid patients with paroxysmal supraventricular tachycardia were treated with radioactive iodine in an attempt to prevent recurrence of the paroxysmal arrhythmias. The production of a relative degree of hypothyroidism appeared to be necessary in order to abolish episodes of supraventricular tachycardias in previously euthyroid patients resistant to other forms of treatment. The mechanism by which such attacks are prevented by suppressing thyroid function is not clear. Of the 25 euthyroid patients treated, 20 obtained good results, 3 fair results and 2 no results. In euthyroid persons with paroxysmal supraventricular tachycardias that do not respond to the usual measures, radioactive iodine may be an effective agent for prevention of further attacks. S. J. SHANE

The Value of Continuous (1 to 10 years) Long-Term Anticoagulant Therapy.

B. MANCHESTER: *Ann. Int. Med.*, 47: 1202, 1957.

The value of continuous anticoagulant therapy was observed during periods of between one and ten years in 712 patients with one or more myocardial infarctions, with the objective of determining the incidence of subsequent infarctions, the mortality, the occurrence of congestive heart failure, and the survival in years per patient. Alternate patients received an oral anticoagulant, and ascorbic acid as a placebo. Blood prothrombin activity was determined once weekly or twice monthly, rarely less often than once per month.

After ten years there remained 404 patients who had co-operated and who had observed the above-described medical regimen without interruption. In both groups, the standard of co-operation, the number of visits required, and the criteria of selection of patients were rigidly observed. The incidence of subsequent myocardial infarctions in the group on anticoagulant therapy was one-third the incidence in the control group. The mortality in the control group was 8 times higher than in the group on anticoagulants. The improvement in survival time in years per patient, and the reduced incidence of congestive heart failure and of thromboembolic complications, are arguments in favour of continuous long-term anticoagulant therapy.

Hæmorrhagic complications occurred in 3% of cases. Bleeding was controlled by the administration of vitamin K_1 without hospitalization. The therapeutic advantages of the use of anticoagulants seem to be more significant than the risk of hæmorrhage.

S. J. SHANE

Leukopenia Associated with Ristocetin (Spontin) Administration.

R. M. NEWTON AND V. G. WARD: *J. A. M. A.*, 166: 1956, 1958.

Two male patients suffered from infection, one with evidence of septicæmia and one with cervical abscess. The administration of ristocetin, a new antibiotic, was beneficial in both cases, but was followed by a fall in the total leukocyte count of 2650 per c.mm. in one case and 1040 in the other. The figures returned to normal after treatment with the antibiotic was discontinued. The clinical and laboratory observations in the two cases are given in detail, and it is suggested that patients receiving ristocetin should be protected against the hazard of leukopenia by having leukocyte counts done frequently, e.g. every other day rather than only once or twice weekly.

S. J. SHANE

Treatment of the Parkinson Syndrome with Aturban *(in German)*.

K. HARTMANN: *Schweiz. med. Wchnschr.*, 88: 474, 1958.

A new anti-Parkinsonian, Aturban, differs from most other atropine-like synthetic products in that it is not an ester; its chemical formula is alpha-phenyl-alpha-(diethylaminoethyl)-glutarimide hydrochloride. The author considers that in spite of the present success with surgical treatment of parkinsonism and with the plethora of drugs for this condition, the introduction of this new product is still worth while. Physicians treating a large number of patients with parkinsonism find themselves having to switch from one drug to another in a certain number of cases for a variety of reasons. Aturban presents a useful addition to the less toxic and yet highly effective drugs in this group. It was used by the author in 111 patients over the past five years and the majority of these patients have continued on the same medication, a fact which in itself speaks for its usefulness. Its best effect is on the rigidity and it causes some improvement of tremor. Side effects and toxicity were not observed even with moderately high dosage. Salivation was somewhat decreased but akinesis remained unchanged. During the past two years the author has been using tablets of Aturban with delayed action and found them most satisfactory. (This drug is under trial in North America under the name Ba-10870, Ciba.)

W. GROBIN

INDUSTRIAL MEDICINE

Hours of Work and Leave Provisions in the USSR.

E. NASH: *Month. Labor Rev.*, 80: 1069, 1957.

In the past two years much new information has become available on provisions for vacations and other forms of leave in the Soviet Union. Such provisions are still set by law and are not subject to collective bargaining or voluntary action by employers.

For most Soviet workers 18 years of age and older, a 46-hour work week is in force. Moreover, the 7-hour day or shift is being gradually introduced in any shop or plant that can still meet its normal production quota. The length of the workday for industrial trainees has also been reduced. As about 75% of industrial workers are on piece-work, the reduction of hours from 48 to 46 may have reduced proportionately their take-home pay.

Overtime work without "permission" of trade union and public authorities is forbidden by law. Overtime and nightwork by workers under 18 years of age and by expectant and nursing mothers is also forbidden, except that expectant workers may work overtime during the first four months of pregnancy.

As a rule workers are entitled by law, after 11 months' continuous service in an enterprise with a legitimate excuse for every absence, to a minimum annual continuous vacation with pay of two weeks (12 workdays). Extra days with pay are given to workers in arduous and hazardous jobs. In order to maintain continued production, 8 to 9% of workers are on vacation each month. Vacations may be postponed for various reasons, but may not be accumulated for more than two years except by workers in the Far North.

Provisions have been made also whereby special leave is granted to workers for annual or semester examinations in connection with correspondence and evening school courses.

Soviet workers may take sick leave only with a doctor's permission, in the form of a sickness certificate. Following a decree of early 1957, a worker is entitled to benefits from the first day of incapacity until he returns to work or is declared an invalid. There are special pensions for invalids. As of February 1, 1957, workers temporarily disabled by a work injury or by occupational disease are entitled to benefits equal to 100% of wages for the period of disability, regardless of length of service or whether they are trade union members. On April 1, 1956, the period of maternity leave was increased. While on leave, women are entitled to free medical care and to regular payments from the State social insurance funds.

MARGARET H. WILTON

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OBITUARIES

DR. ALFRED TURNER BAZIN, aged 85, died on September 3. He was born and educated in Montreal and studied medicine at McGill University. During the First World War he commanded the No. 9 Field Ambulance and the No. 3 General Hospital, and in 1918 he was awarded the D.S.O. In the Second World War he organized a top-secret special assistance group for victims of submarine sinkings, and was active in Red Cross work. Dr. Bazin was appointed a McGill University professor in 1924 and became head of the surgery department in 1938. At the time of his death he was emeritus professor of surgery. He was a past president of the Montreal Medico-Chirurgical Society and of the Canadian Medical Association, which in 1951 awarded him the Starr Memorial Award for distinguished service to medicine.

Dr. Bazin is survived by his widow, a son and two daughters.

DR. ALFRED TURNER BAZIN

AN APPRECIATION

With the death of Dr. A. T. Bazin on September 3, 1958, Canadian medicine lost a great man, one who added lustre to his profession and gave devoted service to his country and his fellow citizens.

Even a comprehensive review of his interests and achievements would not quite tell us of the real quality of the man. That is more truly reflected in the esteem and affection of the multitudes he guided by his teaching, benefited by his professional skill, and influenced by his sound judgment and counsel.

Alfred Turner Bazin was born in Montreal in 1872; was educated at the Montreal High School, and graduated in medicine at McGill University in 1894. After a year's internship at the Montreal General Hospital he became its medical superintendent in 1895. He received his appointment to the surgical outpatient department in 1905 and became surgeon to the hospital in 1912, a post he held until his retirement to the Consultant Staff in 1938.

In 1915 he went overseas on active service with No. 9 Canadian Field Ambulance, and later commanded the unit. Later still he was appointed officer in charge of surgery at No. 3 Canadian General Hospital. He was awarded the D.S.O. and was twice mentioned in despatches.

In 1924 he became professor of surgery at McGill, and was made emeritus professor on his retirement from active teaching in 1938.

He also played a leading part in the administration and development of the Montreal General Hospital. He was secretary of the Medical Board from 1923 to 1928, and an active member of the Board for several years afterwards. This was an extremely active stage of growth in the hospital, during which the Western Hospital was taken over as the Western Division, and the Private Patients Pavilion was built.

With the reorganization of the Canadian Medical Association in the early 'twenties he soon joined the Montreal representatives (Martin, Blackader, Archibald, Scane, etc.) in helping, with infinite labour and patience, to develop organized medicine in Canada. Dr. Bazin was chosen president of the Canadian Medical Association in 1928, and later was made a senior member. In 1951 he was awarded the Starr Memorial Award of the Association in recognition of his distinguished services in medicine. He was also managing editor of the Association's *Journal* and treasurer of the Association for several years. He was an active member and past-president of the Montreal Medico-Chirurgical Society.

From 1924-1926 he was president of the Graduates Society of McGill University, and it was at his instance that the Society's official publication was reorganized and a regular editor appointed.

His energy found yet other outlets for useful public service. At the beginning of World War II, in 1939, with no military medical work available to him, and at an age when many might have considered reducing their activities he became absorbed in the work of the Canadian Red Cross Society, and soon he was devoting much of his time to it. He was responsible for setting up an organization to care for sufferers in ship sinkings in the River and Gulf of St. Lawrence; he edited the Red Cross book of first aid; he was co-chairman for years of the Provincial Red Cross Disaster Preparedness and Relief Committee, and was also in charge of the organization's swimming and water safety program. Enlisting the help of a prominent engineer "retired" like himself, he helped to transform conditions in the Magdalen Islands, establishing outpost nursing stations and organizing medical and dental clinics.

In his later years Dr. Bazin's experience in teaching was recognized in the lay world, and he was asked to act on the Board of Governors of Lower Canada College, where his wise advice was highly valued.

At the age of 80 physical disabilities curbed many of his occupations, but he still visited the hospital regularly, where he was frequently called on for guidance in various committees.

What of the man himself who carried on this long life of industry and fine achievement?

To those of us who knew him in his prime, though even through the eyes of juniors, he remained to his latest days the same extraordinary personality, vigorous, methodical, ever demanding careful, honest work, and yet, for all his intense concentration, always ready to enter into the interests of his younger colleagues. Many men have friends much younger than themselves, but not many manage as did Dr. Bazin, to keep fresh the friendships of his juniors until so late in life.

He was a strong personality, and his life was not free from combatancy. He always spoke his mind plainly and fearlessly, and if he made mistakes they were those of one who wanted to do more rather than less.

Dr. Bazin was a man of many interests, but these had a dominating element in common; they were all concerned with the welfare of the community. Only thus could he satisfy his desire for beneficence through coordinated effort. He taught large numbers of students; his professional work included not only his private patients but the management of a large surgical service as well as hospital administrative work; he rose to the highest positions in surgical teaching, and to the highest honours in organized medicine; his work in the Canadian Red Cross Society alone would have fully occupied the ordinary man. All these things meant numberless committee meetings, but he never failed to fit them in.

Dr. Bazin's first appointment in the Montreal General Hospital was in the surgical out-patient depart-

ment—that rich mine of experience. But this was in a period when men did not specialize so rigidly, and for several years he carried on a general practice as well; indeed it was in general practice that he laid the foundations of his brilliant surgical career and from it that he derived the precepts of common sense which guided him in his work. In his estimation surgery was only a form of therapy. He always felt that the training of a surgeon should be basic in medicine first; the handicraft could come afterwards.

But he also claimed to be a good nurse. He took pride in saying this, and when one saw the exact and copious directions he would write out for postoperative care, his use of drugs, his supervision of the diet, the physical handling of the patient, and all the minutiæ surrounding the care of the sick, one realized that his claim was fully justified. This deep thoughtfulness over the well-being of the patient in every detail he practised with never-failing solicitude. It was as if he had in mind

> Give all thou canst; high heaven rejects the lore
> Of nicely calculated less or more.

In that spirit he spent himself on his patients and helped his friends and colleagues. He has left a deep and widespread influence for good.

H. E. MACDERMOT

DR. CHARLES TELESPHORE FINK, aged 65, died on August 20 in Pembroke hospital following a brief illness. He was born at Mattawa, Ont., and received his primary education at Mattawa, after which he attended the University of Ottawa and St. Francis Xavier University at Antigonish, N.S. He graduated from McGill University in 1921 with the degree of Doctor of Medicine. Following his graduation he practised in Pembroke until 1928, when he moved to Ottawa where he resided for 30 years. During World War II he was a medical officer of the C.O.T.C. at the University of Ottawa.

Dr. Fink is survived by his second wife, four sons and three daughters.

DR. JAMES WILFRID LONG died at his home in Pembroke, Ont., on August 25. He was born at East Dalhousie in 1917, and attended local schools, later graduating from St. Francis Xavier University, Antigonish, N.S., in 1937 with a B.Sc. In 1942, he graduated M.D.C.M. from Dalhousie University in Halifax. He interned at Saint John General Hospital in Saint John, N.B., Royal Victoria Hospital, Montreal, Toronto General Hospital and St. Michael's Hospital in Toronto. From 1945 to 1949 he practised medicine in Brantford, Ont., and Lestock, Sask. Dr. Long received his Fellowship of the Royal College of Surgeons in Toronto in 1951, and in 1952 his Fellowship of the American College of Surgeons.

He is survived by his widow and two sons.

DR. GEORGE EDWARD ROBERT McCARTNEY, aged 78, died on August 8, at his home in Fort William, Ont. He was born in Fingal, Ont., and attended the faculty of medicine of the University of Toronto, graduating with honours in 1901. After his graduation he spent three years interning in various New York hospitals, going to Fort William in 1904. Dr. McCartney rapidly became one of the Lakehead's leading surgeons, and was an active member of the McKellar Hospital until his last illness. He was a charter member of the American College of Surgeons, and in 1947 was made a life member of the Ontario Medical Association. In 1954 he was named a senior member of the Canadian Medical Association.

His second interest was in military-medical affairs. He was a medical student at the time of the South African War, and in the spring of 1915, he went to England where he joined the R.A.M.C., seeing duty on hospital ships and evacuating wounded from the Dardanelles. After a period in Egypt, Dr. McCartney was transferred to Salonica and was medical officer of the Middlesex Regiment on the Struma front. In 1916 he was transferred to England, becoming one of the senior surgeons of the Canadian Hospital at Taplow. In 1919, he returned to his practice in Fort William, Ont.

Dr. McCartney is survived by one son and two daughters.

DR. EMERSON J. TROW

AN APPRECIATION

Emerson J. Trow, M.D., F.R.C.P.[C.], died in Toronto on July 24, 1958. Dr. Trow was one of four Canadian dermatologists who met informally in London, Ont., in 1942 and planned what was to develop into the Canadian Dermatological Association. He served this society loyally throughout the years, holding the office of Secretary and later President. He seldom missed a meeting and his advice and guidance was much sought after. With his pleasing personality, warm smile and tactful diplomacy he was at his best in smoothing over difficult situations.

We looked forward to seeing Dr. Trow at the annual meeting and we especially enjoyed the many informal social gatherings at which he presided. In June of this year at the Annual Meeting, he was elected to Senior Membership in the society of which he was one of the founders and one of its champions through the years. Emmy Trow will be sorely missed by all who were fortunate enough to have known him. R.R.F.

FORTHCOMING MEETINGS

CANADA

THE CANADIAN SOCIETY FOR THE STUDY OF FERTILITY, Fifth Annual Meeting, London, Ont. (Dr. Jean F. Campbell, Secretary-Treasurer, 238 Queen's Avenue, London, Ont.) October 31 and November 1, 1958.

UNITED STATES

THE ACADEMY OF PSYCHOSOMATIC MEDICINE, Fifth Annual Meeting, New York, N.Y. (Dr. Bertram B. Moss, 55 E. Washington, Suite 1035, Chicago 2, Ill.) October 9-11, 1958.

INTER-SOCIETY CYTOLOGY COUNCIL, Annual Scientific Meeting. Hotel Statler, New York, N.Y. (Dr. Paul F. Fletcher, Secretary, 634 North Grand Avenue, St. Louis 3, Missouri.) November 13-15, 1958.

INTERNATIONAL ANESTHESIA RESEARCH SOCIETY, 33rd Congress, Miami Beach, Florida. (Dr. A. William Friend, Executive Secretary, Wade Park Manor, East 107 and Park Lane, Cleveland 6, Ohio.) April 20-23, 1959.

OTHER COUNTRIES

SIXTH BAHAMAS CLINICAL CONFERENCE, Nassau, Bahamas. (Dr. B. L. Frank, Box 1718, Nassau.) December 1-15, 1958.

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PROVINCIAL NEWS

BRITISH COLUMBIA

British Columbia this year has had probably the hottest and driest summer it has ever known – and this has resulted in forest fires, costing the province many millions of dollars, loss of crops, closure of forests to lumbermen, hunters and visitors; in general, this has been a hard year.

Added to this is a record number of strikes by labour, which have tied up all B.C.'s ports – and resulted in stoppage of work on over fifty million dollars of work in Vancouver alone. One very large project, the new Centennial Pavilion of the Vancouver General Hospital, has been stopped by the electricians' and plumbers' strike, which has affected other hospital buildings, the new auditorium in Vancouver, many new apartment buildings, and several new schools. This has led to much grief amongst school boards, as well as amongst parents.

Added to all this is the closure of all the swimming beaches, owing to excessive pollution. The beaches are definitely closed, only a few regulated and chlorinated pools being left open.

We mention all this to show that B.C. is suffering from a severe economic obstruction, and it is earnestly hoped that this obstruction will be speedily relieved. We read of cities, e.g. Victoria, having to find sums for indigent relief – a thing that has not been known for many years.

The City of Vancouver is planning, through the Greater Vancouver Sewage Board, to instal a complete system whereby sewage will be all diverted to a point in the Fraser River, and treated to harmlessness. It is hoped that this will be speedily done.

The Medical Health Officer of the Metropolitan Area of the Lower Mainland reports that a bat sent to U.B.C. from the Okanagan was found to have rabies. A North Vancouver man was reported bitten by a bat, but neither he nor the bat has been located.

October 6-10 will be busy days in Kelowna, where the B.C. Division of the C.M.A. holds its Annual Meeting at that time.

The B.C. College of Physicians and Surgeons also holds its Annual Meeting then, and Dr. W. J. Knox, dean of the medical profession of the Okanagan, will be guest speaker at this. Dr. Knox is known and beloved throughout the Okanagan, and no more popular choice could have been made. A strong clinical program has been arranged, and should be most attractive. Most generous provision has been made for entertainment – golf, luncheons, dinners, etc. – and the Ladies' Entertainment Committee is taking good care of our wives and daughters who are accompanying us.

J. H. MACDERMOT

SASKATCHEWAN

Dr. John Orr, the General Superintendent and Medical Director of the Saskatchewan Tuberculosis League, reported at the 44th Annual Meeting of the League, held in Prince Albert, that although 212 new cases of tuberculosis were discovered in Saskatchewan in 1957, a new low death rate of 3.5 per 100,000 population was achieved. "With fewer patients to treat and with empty beds the tuberculosis picture in this province was never so bright as now," he said, "but the progress carried with it additional administrative and financial problems as services had to be maintained."

Dr. Orr noted that there were only 31 tuberculosis deaths in the province last year. Of the 26 white persons who died none was listed below 18 years of age. In 1937 there were 54 children under 10 out of a total mortality of 296. Last year five Indian people died of tuberculosis; of these, three were children under 9 years of age. The 212 new cases discovered were only 5 fewer than in 1956, but the favourable trend of three previous years continued. Thirty-nine new cases were found in the League's mass surveys. Overall attendance at mass surveys was more than 80%. The relative age of patients has changed; the number of persons 70 years or older admitted 10 years ago was 2% of new admissions. In 1957 this had changed to more than 14%.

In conclusion Dr. Orr noted that the preventive program which had been the basis of the League's progress in battling tuberculosis here must be continued if the favourable position was to be maintained and new gains added.

G. W. PEACOCK

MANITOBA

Dr. Jonathan E. Rhoads, Professor of Surgery at the University of Pennsylvania, will address the annual meeting of the Manitoba Chapter, American College of Surgeons, on December 13.

Dr. Leslie Kasza has been appointed to the medical staff of the Manitoba Sanatorium as senior intern. He is a graduate of the University of Szeged, Hungary, and for the past year has been an intern at Misericordia General Hospital, Winnipeg.

ROSS MITCHELL

ONTARIO

The Princess Margaret Hospital, home of the Ontario Cancer Institute in Toronto, was officially opened by the Lieutenant Governor, the Honourable John Keiller MacKay, on Thursday, September 25. Also present were the Prime Minister, the Right Hon. Leslie M. Frost, and religious and civic leaders. The hospital which cost seven million dollars to build and occupies seven storeys on Sherbourne Street is one of the best equipped in the world for dealing with cancer. It was built by the Ontario Government, contains 87 beds, and is one of eight cancer treatment and research centres in the province sponsored by the Ontario Cancer Treatment and Research Foundation. About 75% of its space is for the care of patients suffering from cancer and related diseases, the remaining 25% being devoted to research. An adjacent 53-bed hostel for out-of-town patients coming for daily treatment will be opened shortly.

The Institute is one of the University of Toronto group of teaching hospitals and is directed by Dr. C. L. Ash, with Dr. O. H. Warwick as senior physician. The division of biological research is headed by Dr. A. Ham, the division of physics by Dr. H. E. Johns, and the division of hospital services by Mr. John F. Law.

here's a patient who will probably benefit from weight reduction

the overweight hypertensive

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BOOK REVIEWS

UNDERSTANDING YOUR PATIENT. Edited by Samuel Liebman, Medical Director, North Shore Hospital, Winnetka, Ill. 170 pp. J. B. Lippincott Company, Philadelphia and Montreal, 1957. $5.00.

The idea behind this volume is to assist the physician in facilitating recognition of emotional problems and in establishing an understanding approach to them. Most of the book consists of a series of essays on emotional problems at various ages—in the baby, the school-age child, the teenager, the adult, the person about to be married, the married, and the grandparent. These essays follow sound lines, and would be helpful to any physician wishing to learn more about the emotional problems of his patients—and this should include all general practitioners.

The volume begins with two interesting and unusual essays. The first one is by Daniel Blain, who discusses the unique position of the physician in our society. He makes the point that in the final analysis it is society or the public which defines the position of a physician. Whereas, in the past, society has accorded to the medical profession a most honourable place in its ranks, it must not be taken for granted that this will continue. Blain analyzes a number of answers given by intelligent persons to questions designed to discover what the public felt about the adequacy of doctors in meeting the emotional needs of people. There seemed to be a general awareness that physicians could do and were trying to do a better job of meeting these emotional needs. The second essay is equally informative, and deals with psychological preparation of the individual for medical and surgical care. This again is a field which many physicians could learn more about with profit.

THE CHEMISTRY AND CHEMOTHERAPY OF TUBERCULOSIS. E. R. Long, University of Pennsylvania. 450 pp. 3rd ed. The Williams & Wilkins Company, Baltimore, Md.; Burns & MacEachern, Toronto, 1958. $12.00.

This is a new edition of the volume originally entitled "The Chemistry of Tuberculosis", which first appeared in 1923 and was written by H. Gideon Wells, Lydia M. DeWitt and the present writer. The second edition appeared nine years later, during which interval Dr. DeWitt had died, leaving that edition to be prepared by Drs. Wells and Long. Between 1932 and 1958, Dr. Wells also passed away, and the present edition is prepared by Dr. Long alone. The new title mirrors the revolutionary changes that have taken place in our knowledge of tuberculosis during the past quarter-century, and the book is now divided into three section: (1) Chemistry of Tubercle Bacilli; (2) Chemical Changes in the Tuberculous Host; and (3) Chemotherapy of Tuberculosis.

Certain important but not crucial changes have taken place in the purely chemical aspects of the tuberculosis problem since the last edition, but these mostly concern the development of new culture media, etc., and it would appear that present concepts of the chemistry of *M. tuberculosis* are little different from what they were 25 years ago. A new feature is the growth of tubercle bacilli *in vivo*, particularly in tissue culture on HeLa cells which may in later years prove to be of some special importance.

The section on chemical changes in the tuberculous host also contains no startling surprises; but it should be emphasized that we still have no accurate knowledge of the basic cause of caseation and the true nature of the caseum. Also, Dr. Long brings us up to date on the as yet little-understood effects of steroid hormones on human cellular biochemistry, particularly as affected by the tubercle bacilli.

It is, of course, the section on chemotherapy that is the newest addition, and to some the most interesting one. In this section, Dr. Long discusses all the antibiotics and chemotherapeutic agents that have been and are still being used in the treatment of tuberculosis, including the steroid hormones, and provides the interested reader with a clear, lucid and unbiased evaluation of each.

The book is stated to be a "compilation and critical review of existing knowledge of the chemistry of tubercle bacilli and their products, chemical changes and processes in the host, and chemical aspects of the treatment of tuberculosis". It is not claimed that it promulgates any new theories or takes sides in any controversial issues. In its professed objectives this new edition succeeds admirably and should become part of the library of every thoughtful and practical student of tuberculosis.

The printing and paper stock are excellent and the bibliography is encyclopædic.

SIR CHARLES BELL—HIS LIFE AND TIMES. Sir G. Gordon-Taylor and E. W. Walls. 288 pp. Illust. E. & S. Livingstone Ltd., Edinburgh and London, 1958. 42s.

It is appropriate that a book about a Scottish romantic who found fame—though not fortune—in London should have as its senior author another Scottish romantic of a later vintage but of equal fame.

This is a biography of which Sir Walter Scott would have approved and Lytton Strachey with his clever and uncharitable pen would have heartily disapproved, for as the biographers tartly remark, "The modern reader will doubtless regret that no amount of psychiatric research has revealed Charles Bell as a philanderer or demonstrated that the affectionate letters which he wrote to his wife were those of a hypocrite."

Sir Charles Bell (1774-1842) was a native of Edinburgh who made his reputation in Edinburgh as an anatomist, surgeon and artist, ran Hunter's school of anatomy and subsequently helped to found the Middlesex Hospital. At the age of 62, driven no doubt by that nostalgia which is prone to attack ageing Scottish exiles, he accepted the chair of surgery in the University of Edinburgh and spent his few remaining years in comparative poverty. The modern world would deem him unsuccessful, for he never made a fortune; but his biographers know better, and show how his qualities of kindliness and devotion to teaching, writing and research militated against material success. This very kindliness prevented his being a surgical giant in a brutal age, or a top-flight physiologist in an era of vivisection without benefit of anæsthesia.

Bell's chief claim to fame is generally considered to lie in the establishment of the motor and sensory functions of the spinal nerves; about this a bitter controversy has raged for many years. Has Bell or Magendie the priority in this discovery? The authors present the facts fairly and do not hide from the

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reader that Bell behaved somewhat badly over the whole business. Incidentally they reproduce the relevant documents in the case.

They also show Bell's skill as an artist, giving some beautiful illustrations of his work. His patriotism is demonstrated by a description of the two episodes when he left his London work to treat the wounded from Corunna and those from Waterloo. His capacity for inspiring devotion is equally well demonstrated throughout the book, particularly in his relationship to his pupil John Shaw.

He was a man of parts, indeed of so many parts and activities that even in an age of versatility he missed the highest rank by attempting too much in too many fields. This affectionate biography will bring fresh admirers to a personage so neglected that his grave was utterly lost to sight for many years.

OPERATING ROOM MANUAL: A Guide for O.R. Personnel. M. E. Yeager. 213 pp. Illust. G. P. Putnam's Sons, New York; McAinsh & Company, Limited, Toronto, 1958. $4.50.

This is an extensive and detailed publication concerned mainly with the requisite sterile and unsterile supplies for many operations in the various fields of surgery. It might be a helpful reference for operating-room staff when it is necessary to prepare for some operation with which they have had no previous experience.

However, the manual is so detailed and specific that its greatest value is probably within the particular operating-room in which the author has had most of her own experience. Rarely does one find a similar arrangement in two operating-rooms, or the same needles and sutures being used for the same operative procedures.

MARTIUS' GYNECOLOGICAL OPERATIONS. Translated and edited by Milton L. McCall, Department of Obstetrics and Gynecology, Louisiana State University School of Medicine, New Orleans, and Karl A. Bolten. 405 pp. Illust. Little, Brown & Company, Boston, Mass.; J. B. Lippincott Company, Montreal, 1956. $20.00.

The purpose of this book is to set forth the anatomical basis of surgical technique. It does not stray from this point to bog down in excessive or redundant detail or to include preparative and postoperative care. Four hundred and fifty drawings of great clarity and simplicity illustrate step by step processes. Never is the point of the drawing or orientation lost.

Topographic anatomy is stressed, as are the variations in surgical anatomy of techniques when these are altered by the variations of pelvic disease processes.

This is the second translation of a leading continental text. Professor Martius is the head of the University Clinic for Women in Gœttingen. The translation and editing of this issue is by Professor Milton L. McCall and Dr. Karl Bolten of New Orleans. The text is simple and is quite sufficient to amplify the drawings, which number just over one to the page.

Flexibility in operative technique is stressed, depending on the pathological findings under anæsthesia or at laparotomy. The drawings are good models of operative techniques, and as such excellent material for undergraduate or postgraduate teaching. This book would be a useful addition to every hospital library.

REGIONAL ILEITIS. B. B. Crohn and H. Yarnis, New York. 239 pp. Illust. 2nd ed., revised. Grune & Stratton, Inc., New York, 1958. $7.25.

The first edition of this monograph on Crohn's disease discussed an experience with 300 cases. Nine years later, another edition is based on private patients to the number of 542 cases of regional terminal ileitis, 70 of diffuse ileo-jejunitis and 64 combined ileo-colitis. Thus it is over 25 years since Crohn, Ginzburg and Oppenheimer presented the original paper—time for an evaluation of a lesion which has become a not uncommon clinical entity. There are 327 references listed.

It is noteworthy that Crohn considers the disease to have been described by Morgagni in the 18th century, Combe and Saunders in 1813, John Abercrombie in 1828, and Moynihan in 1907, as well as others before him. No age, race or social position is known to be immune. Etiology is not known though many theories have been advocated. Surgery seems most useful in the third year of the disease on an average. The favoured operation for terminal ileitis is transection of the ileum and ileo-colostomy.

Though no longer rare, regional ileitis is not likely to be seen very often by any one doctor. The diagnosis must be frequently missed; this will not happen so often if this book is widely read. The presenting symptom of intermittent diarrhœa, or perianal fistula, or abdominal pain, or anæmia may lead to the diagnosis. The differential diagnosis, etiology, treatment and indications for surgical intervention as well as the radiological diagnosis and the prognosis are fully covered.

"Regional Ileitis" is a valuable addition to any medical library.

ELECTROCARDIOGRAPHIC ANALYSIS: Vol. I, BIOPHYSICAL PRINCIPLES OF ELECTROCARDIOGRAPHY. R. H. Bayley, University of Oklahoma. 237 pp. Illust. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York, 1958. $8.00.

Before the Second World War it would have been impossible to find in any one place, particularly in a book, a detailed account of the biophysics of electrocardiography. Since then a number of publications containing this sort of information have appeared, partly because of the increase in our knowledge of the subject and partly because of a more lively and intelligent interest in its basic principles. The present book is the first of a pair of volumes, of which the second will be devoted solely to the clinical aspects of electrocardiography. The author is well known in the realm of experimental and theoretical electrocardiography.

The first chapter deals with the electrical fields and leads, the second with the excitation of the fibre, and the third with vectors. Depolarization in normal and abnormal states is described. One chapter is devoted to T wave changes and one to currents of injury. The more difficult mathematics is reserved for the final chapter. A useful glossary is appended.

Some of the author's concepts are at variance with those of other authorities, but this is what one expects in a difficult and growing field. This is not a book for the dilettante but it will repay careful study by anyone interested in the fundamentals of electrocardiography.

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TUBERCULOSIS IN WHITE AND NEGRO CHILDREN. Vol. I: The Roentgenologic Aspects of the Harriet Lane Study. J. B. Hardy. 119 pp. Illust. Vol. II: The Epidemiologic Aspects of the Harriet Lane Study. M. E. Brailey. 103 pp. Published for The Commonwealth Fund by Harvard University Press, Cambridge, Mass.; S. J. Reginald Saunders and Company Limited, Toronto, 1958. Vol. I $8.25, Vol. II $4.95.

The Harriet Lane Study originated in Baltimore in 1928 in a special out-patient clinic for young children already infected with tuberculosis, or members of households containing an adult with positive sputum. The records for analysis in this study include those of all infants admitted to the clinic for demonstrated infection plus those of their elder brothers and sisters who were not yet 15 years of age when tuberculosis was discovered. The period of study extended between 1928 and 1944, with follow-up study to 1950 in each case, unless death occurred before that time. The material for study thus included the records of 437 white and 892 Negro children who fit the above criteria.

The first volume consists of a large number of chest roentgenograms with brief clinical descriptions appended. These were chosen to illustrate the various phases of tuberculosis in children, as demonstrated by x-ray. Some of the conditions that enter into the differential diagnosis of tuberculosis and other conditions are also included. This material is set out in serial fashion and demonstrates the sequential changes in tuberculous infections in children, both before and during the era of antimicrobial therapy. In the reviewer's opinion, the reproductions are excellent, and the authors and publishers are to be commended for the unusual preservation of roentgenographic detail, a feature which usually suffers in publications of this type. In addition, this volume also contains a section on bronchoscopic and bronchographic techniques in children, which, taken in conjunction with the beautifully reproduced roentgenograms, adds to the value of both.

The second volume consists of epidemiologic studies, based on the experience at the Harriet Lane Tuberculosis Clinic before antimicrobial therapy for tuberculosis came into use. As such, it is of special value since it answers several hitherto unclarified questions about the natural history of childhood tuberculosis which have since become clouded by the introduction of widespread antimicrobial therapy. This volume is divided into two sections—Section I dealing with the prognosis of primary tuberculous infection in children, and Section II assessing the risk of developing progressive pulmonary tuberculosis of the reinfection type. Both these sections contain a wealth of information of interest and value to the epidemiologist, but the most striking finding merely corroborates previous impressions of the serious import of tuberculosis in Negro as compared to white children. It would appear that Negro children, roughly speaking, suffer from a twofold to eightfold higher mortality than white children after the discovery of primary tuberculosis, depending on their age, the length of the study period and the presence or absence of demonstrable pulmonary infiltrations. Among other features the study shows that, other things being equal, Negro children who have had a primary tuberculous infection are three times as likely to suffer from superinfection after suitable exposure as are white children. These figures, of course, have been and will continue to be greatly modified by the present rapidly increasing tendency to provide effective antimicrobial therapy at the earliest possible time after infection. Their major value lies in the fact that they point up the importance of early antimicrobial therapy in the presence of a demonstrated or strongly suspected primary infection or superinfection.

This feature, together with the high educational value of the roentgenograms in Volume I, renders it almost mandatory that these volumes be on the bookshelves of all those interested in the treatment and control of tuberculosis.

SPEZIELLE CHIRURGISCHE THERAPIE (Special Surgical Therapy). Max Sägesser. 1476 pp. Illust. 5th ed., revised and enlarged. Medizinischer Verlag Hans Huber, Bern and Stuttgart, 1958. Fr. 128–.

There are a few textbooks which leave the reader awed by the immense range of knowledge displayed, and the expenditure of energy involved in their writing.

Saegesser's book is one of the phenomena; there is no other word for it, since he has apparently single-handed covered the whole range of surgical treatment including fractures, and covered it thoroughly. The book has proved very popular in Germany and Switzerland, for this is its fifth edition in 10 years. It is notable for the clarity and detail of its approach. Saegesser does not leave his reader out on a limb. He tells him exactly what he should do in every type of situation, often how to make his diagnosis, and what the anatomical and pathological bases for his treatment are. Obviously this dogmatism has its drawbacks, but for the young and perplexed surgeon who needs urgent help and not philosophy, one can see the great virtue of this type of approach. In some cases Saegesser has strong and individual views on treatment, but he also quotes freely from the literature.

It should be added that the German style is easy and lucid, and the illustrations are profuse and more than adequate. The book reveals Swiss typography and publishing art at its finest — and that is very fine indeed.

MEDICINE AND THE NAVY 1200-1900: Volume I—1200-1649. J. J. Keevil. 255 pp. Illust. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1957. $6.75.

It is regrettable that the untimely death of Surgeon Commander Keevil has robbed us of a portion of a history of naval medicine, of which this is the first volume. The work was undertaken as a comprehensive survey of the subject, but over the span (1200-1649) covered by the first volume this means mainly an account of the rise of medical services in the Royal Navy.

Medical (or rather surgical) services were slow to develop because voyages were short and sailors were not supposed to fight in naval battles. Wounded soldiers aboard were landed for treatment in the event of victory, or thrown overboard by the victors if captured. The status of medical men was low, for Henry V classified them with shoemakers and washerwomen, and Edward III's apothecary was mainly useful in preparing gunpowder.

The ship's surgeon appeared in Elizabethan times, but was often a poor specimen, for the press gang

(Continued on page 610)

(Continued from page 608)

was the chief means of recruitment. It is, however, pleasing to note that, when physicians began to appear on ships, Queen Elizabeth ordered a future president of the College of Physicians of London to replace a similarly conscripted and very seasick royal physician on a naval expedition.

Several themes run through this book. One is the eternal one of the fatal consequences of disunity within the medical profession. If, for example, the sea surgeons of the sixteenth century had also been trained in internal medicine or permitted to practise it, much of their knowledge of tropical diseases would have been properly collated and applied at an early date. Another theme, related to the first, is the exasperating way in which cures for such common scourges as scurvy and other basic clinical facts kept being discovered and then forgotten. For example, Richard Hawkyns in 1593 understood the use of oranges and lemons in scurvy, while Henry Hawks in 1572 correctly traced malaria to mosquito bites.

With the coming of the seventeenth century, medical and surgical services at sea began to be properly organized, and the rise of the middle class in England, followed by an increase in general practice, made a supply of more competent men available. In 1626, ships began to carry drugs, and in 1617, Woodall wrote *The Surgeon's Mate* as a guide to ship surgeons, while Captain John Smith defined their duties a little later. The interesting point is that, inadequate as their services must have been, the surgeons were already held in esteem by the crew.

At the close of the book, the Royal Navy is in poor shape through the neglect of the early Stuarts, but the foundations have been laid for the effective medical services of the years to come.

DR. W. C. ROENTGEN. O. Glasser. 169 pp. Illust. 2nd ed. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1958. $5.00.

In 1945, the centenary of Roentgen was celebrated, and various American radiological societies sponsored a commemorative volume containing a new translation of Roentgen's three classic papers on "A New Kind of Rays". Dr. Glasser has now produced a second edition, with some few modifications, of the biography he wrote in 1945, incorporating the three papers. This remains a reliable shorter biography of the father of radiology.

MEDICAL TELEOLOGY AND MISCELLANEOUS SUBJECTS. F. Parkes Weber. 86 pp. H. K. Lewis & Co. Ltd., London, 1958. 15s.

This is the last collected series of notes and essays from the pen of a most unusual man, known to many principally as a collector of rare diseases and a writer on unusual medical subjects. The first part of the book consists of reprints of pre-war writings on teleology in relation to medicine, such as his view that humanity is divided into high-pressure and low-pressure individuals with safety valves set at different levels for the two groups. The rest is a very mixed bag of odd writings on disease, symptoms, coin-collecting and history. It is full of curiosities, such as the author's use of quinine to keep himself awake after lunch, and his description of a hypoglycæmic attack on top of a mountain.

DER SUICID: Unter besonderer Berücksichtigung Versorgungsärztlicher Gesichtspunkte (Suicide: With Special Regard to the Medical Aspects of Compensation). Fred Dubitscher, Cologne. 224 pp. Illust. Georg Thieme Verlag, Stuttgart; Intercontinental Medical Book Corporation, New York, 1957. $3.95.

This monograph is part of a series of publications on social aspects of medicine. It deals with suicide mostly from the legal-administrative angle, with special emphasis on the problems of compensation. Built around this main theme, however, a concise but extensive presentation of the entire subject is given. The point of departure is the statement by the author that suicide as a phenomenon is always related to the place of its occurrence. This, therefore, is the frame of reference in which the problem can be analyzed, and should be reviewed time and again within the changing framework.

The last decade with World War II in the centre, and the German scene, form the setting in which the author of this monograph analyzes the problem. The introductory chapter is a scholarly account of the cultural history and the social anthropology of suicide. A discussion of areas of research follows: attempts to classify suicide, statistical presentation of relevant data, and psychological studies on motivation. The author's own research was based on case histories, legal documents and insurance files of 3208 cases. Inherent and environmental precipitating factors are analyzed.

The majority of the material on which this study is based dates from the war period; in fact, most of the persons were in active military service at the time of their suicide or were ex-soldiers of the German Army. The author points out that the constellation of factors in his case material is very different from that collected in peacetime populations. Similarities and differences between previous works and the author's own observations are presented and discussed (e.g. spring-time peak in incidence was seen during war as in peace; being married, however, was not a protective factor under wartime conditions). The final sections of this volume give a concise discussion of the presuicidal syndrome and the prophylaxis of suicide.

This monograph is a valuable guide for those interested in the medico-legal and the compensation aspects of suicide. For those with a special interest in the study of suicide this work presents data collected under unique circumstances. These particular advantages, however, make this volume rather too specialized for the general reader.

LEHRBUCH DER GYNÆKOLOGIE (Textbook of Gynæcology). H. Martius, Göttingen. 426 pp. Illust. 5th ed., revised. Georg Thieme Verlag, Stuttgart; Intercontinental Medical Book Corporation, New York, 1958. $11.85.

This excellent standard textbook of gynæcology is probably the best known German one. As might be expected, the most important changes in this new edition are in the field of functional disturbances. The book now begins with a long chapter on disturbances of function and their treatment, but Martius warns against the neglect of thorough gynæcological examination. He constantly sees cases in which neglect to examine the patient thoroughly has led to futile treatment for a supposed functional disorder. The book is unusually well illustrated, for there are over 450 illustrations, some in colour.

Canad. M. A. J.
Oct. 1, 1958, vol. 79

ROENTGENANATOMIE DER NEUGEBORENEN UND SÆUGLINGSLUNGE (Radiological Anatomy of the Lung in the Newborn and Infants). Z. Zsebök, Budapest. 160 pp. Illust. Georg Thieme Verlag, Stuttgart; Intercontinental Medical Book Corporation, New York, 1958. $17.85.

Dr. Zsebök is known in the roentgenological literature as the co-author with K. Kovats, Jr., of the *Roentgen-anatomical Basis of Examination of the Lungs*, a book also translated into French and enjoying great popularity among all interested in pulmonary diseases.

The present work is, to the reviewer's knowledge, the first comprehensive attempt to analyze in a monograph the radiological appearances in the chest of the newborn and of the infant. The author based this study on an analysis of the radiographs of the chest of 150 fetuses from the age of 3 to 10 months; of 1000 mature living newborn, x-rayed within 24-48 hours post partum, of which 200 were examined between the first and the eighth day of life; of 65 fetuses of calves (3-9 months' gestation) and of 50 fetuses of sows (at different periods of gestation).

A historical review of chest and lung investigation is given with reproductions of the various anatomical studies dating back to Willis's description of the lobes of the lung in 1676 and Diemerbroecks's study of anatomy of the bronchial tree in 1665. The various methods of investigation and reproduction of the bronchovascular and of the alveolar tree, including the author's procedures, are discussed at length. One chapter deals with the anthropometry of the chest of the newborn and infant, another with roentgenographic technique. The various constitutional types of the chest are described and illustrated.

Methods of chest and heart measurement are analyzed, and a separate chapter deals with the roentgen anatomy of the bony thoracic cage. The development of the fetal lungs is also discussed in a separate chapter. A detailed study of the anatomy of the bronchial and vascular tree, of the hilar shadows and of the "lung markings" is presented. The roentgen anatomy of the lymphatic system of the chest is exceptionally well described, including the studies of Sukiennikow and Ronvière and the recent thesis of Kubik (Budapest, 1956). The final chapters deal with postnatal pulmonary atelectasis, the thymus gland, the anatomy of the diaphragm and of the pleura. A comprehensive list of references up to 1956 and an index follow the final chapter.

This monograph will be a valuable addition to the radiologist's reference library. It is well written. The publishers are to be congratulated on the excellent reproduction of radiographs and the graphic qualities of this book.

THE YEARBOOK OF MODERN NURSING, 1957-58. A Source Book of Nursing. Edited by M. Cordelia Cowan. 460 pp. G. P. Putnam's Sons, New York; McAinsh & Co., Limited, Toronto, 1958. $9.50.

The series of which this is the second volume has the dual purpose of presenting new thought in the field of nursing and giving a summary of current advances in all aspects of nursing. This volume includes original articles, digests from recent publications and extensive bibliographies. As it is the work of many people who are well known in various fields of nursing and the allied professions, it is a valuable and reliable source book on the broad subject of modern nursing.

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ANNUAL REVIEW OF MEDICINE, Vol. 9, Edited by D. A. Rytand and W. P. Creger, Stanford University School of Medicine. 530 pp. Annual Reviews, Inc., Palo Alto, Cal., 1958.

The present volume begins with reviews of literature on infectious diseases—viral, bacterial and fungal—with particular attention to such difficult problems as staphylococcal infection, the chemotherapy of fungal infections, and the respiratory and intestinal pathogenic viruses. The gastroenterology section contains discussions of all the topical conditions including gastric hæmorrhage and ulcerative colitis. There are separate chapters on medical and surgical cardiovascular and renal diseases, with a short chapter on aortic disease. The hæmorrhagic disorders are reviewed in much detail, and there are also large sections on endocrinology and allergy.

Dr. Cleghorn of Montreal has had the difficult assignment of writing up psychiatry in a dozen pages, and has compressed a great deal on a few selected topics into this space. Psychopharmacology is dealt with separately. Among the many other subjects covered, mention might be made of the timely chapter on toxicology of radioactive materials, Cannon's review of some basic aspects of plastic surgery, a section on paper chromatography and electrophoresis, and a review by a Russian of medical research in the Soviet Union.

THE ALCOHOL LANGUAGE: WITH A SELECTED VOCABULARY. M. Keller and J. R. Seeley. 32 pp. University of Toronto Press, Toronto, 1958. $1.50.

This little book has been published because the authors feel that there is much confusion in terminology about alcohol and alcoholism. The book begins with a short essay by Keller on the language of alcohol, stressing the need for uniform definitions of common terms sometimes used in different senses, and continues with a selected vocabulary of 60 words or so, commonly used in connection with alcohol and alcoholism. Finally, there is a short essay by Seeley on the problems of language in multidisciplinary fields.

At first sight, it may seem surprising that there is a need to define exactly such terms as "sober" or "blackout". However, the compilers of the vocabulary point out that each of these words has two distinct meanings, and it is obviously essential for research records to make clear which meaning they are attaching to the word. Moreover, as Seeley points out, an enormous variety of workers are concerned in problems of alcohol, with a resultant strain on terminology. It is hoped that this will initiate a systematic definition of the more important terms in this specialty.

THE FIRST TEN YEARS OF THE WORLD HEALTH ORGANIZATION. 538 pp. Illust. WHO, Palais des Nations, Geneva, 1958. $5.00.

Considering the many trials and tribulations to which international organizations are subject, this record of the first ten years of the World Health Organization makes encouraging reading. Its Director-General, Dr. M. G. Candau, in his foreword strikes the right note in pointing to the increasing desire of member states to co-operate in the activities of WHO. This is true not only of governments but also of scientific institutions and individuals. All international health workers will require a copy of this well-conceived monograph.

Books Received

Books are acknowledged as received, but in some cases reviews will also be made in later issues.

Klinische Calorimetrie und Thermometrie. Die thermischen Messverfahren zur Registrierung der Haut- und Gewebedurchblutung am Menschen. Grundlagen, Technik, Methodik und Anwenung in Klinik und Praxis (Clinical Calorimetry and Thermometry. The Thermoprocedures for the Measurement of Skin and Tissue Circulation in Man. Bases, Technique, Methods and Application in Hospital and General Practice). H. P. Kuemmerle, Tübingen. 112 pp. Illust. Georg Thieme Verlag, Stuttgart; Intercontinental Medical Book Corporation, New York, 1958. $4.30.

Internationales Symposium ueber Klinische Cytodiagnostik. Vom 1-2. März 1957 in Erlangen (International Symposium on Clinical Cytodiagnosis. March 1 and 2, 1957, at Erlangen). Edited by N. Henning and S. Witte, Erlangen. 216 pp. Illust. Georg Thieme Verlag, Stuttgart; Intercontinental Medical Book Corporation, New York, 1958. $8.10.

Psychiatric Research Reports of the American Psychiatric Association. Edited by Members of the Committee on Research, 1956-57. Research in Psychiatry with Special Reference to Drug Therapy. 181 pp. American Psychiatric Association, Washington, D.C., 1958.

Psychopharmacology. Pharmacologic Effects on Behavior. Vol. III. Progress in Neurobiology. Edited by H. H. Pennes, New York. 362 pp. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York, 1958. $8.00.

Pediatric Surgery. O. Swenson. 740 pp. Appleton-Century-Crofts, Inc., New York, 1958.

Ueber die Erblichkeit des Normalen Elektroencephalogramms. Vergleichende Utersuchungen am ein- und zweieiligen Zwillingen (Inheritance of the Normal Electroecephalogram. Comparative Investigations in Uniovular and Binovular Twins). E. Vogel, Berlin. 92 pp. Illust. Georg Thieme Verlag, Stuttgart; Intercontinental Medical Book Corporation, New York, 1958.

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The Editor reserves the right to make the usual editorial changes in manuscripts; these include such changes as are necessary to ensure correctness of grammar and spelling, clarification of obscurities or conformity to *Journal* style. In no case will major changes be made without prior consultation with the author. Authors will receive galley proofs of articles before publication, and are asked to confine alterations of such proofs to a minimum.

Reprints may be ordered on a form supplied with galley proofs.

References: Authors should limit references to published work to the minimum necessary for guidance to readers wishing to study the subject further. They should not quote articles they have never seen, and should set out references in a numbered list at the end of the article, thus:

1. Doakes, J.: *M. J. Kamchatka*, 1: 2, 1955, giving in order: (1) Author's name and initials in capitals. Where more than three authors are concerned in an article, only the first should be named, with *et al.* as reference to the others. (2) Cumulative Index Medicus abbreviation of journal name. (3) Volume number. (4) Page number. (5) Year.

References to books should be set out as follows:

Pickwick, S., *Textbook of Medicine*, Jones and Jones, London, 1st ed., p. 30, 1955.

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Positions Wanted

ORTHOPÆDIC SURGERY AND TRAUMATOLOGY.—Canadian medical general practitioner, age 33 years, married. Two years' general practice and five years' residency. Now eligible for fellowship examination. Available immediately. Reply to Box 828, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

RADIOLOGIST, Canadian graduate, age 30 years. American boards including nuclear medicine. Writing certification in diagnostic radiology fall 1958 and therapeutic fall 1959. Available January 1, 1959. Reply to Box 844, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

ENGLISH WOMAN DOCTOR (M.R.C.S., L.R.C.P., D.A.) H.P., H.S.: casualty experience, eight years' anæsthesia England, United States and Australia; seeks assistantship, preferably with view, in any reciprocal province, town or country. Available December 1, 1958. Reply to Advertiser, 57 Stubbs Terrace, Daglish, Perth, Western Australia.

BRITISH GRADUATE SURGEON wishes opening in surgical practice in Canada. Age 33 years. F.R.C.S. England and Edinburgh. Graduate of Glasgow university with postgraduate experience in Glasgow and Oxford. At present holds consultant post in a university hospital. Reply to Box 850, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

UROLOGIST, writing certification examinations this fall, is seeking position with another urologist or clinic, preferably in Ontario or Manitoba. Available January 1, 1959. Age 31 years, married with two children. Please reply to Box 853, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

Positions Vacant

FOR OTOLARYNGOLOGIST, excellent unopposed opportunity to establish in British Columbia. Office space available immediately. Modern hospital facilities. Population approximately 35,000. Practising general practitioners 33. Reply to Box 856, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

WANTED: OPHTHALMOLOGIST to assist board certified ophthalmologist in city of 35,000 in northwest part of State of Washington. Pleasant environment. Eventual partnership. Should be well-qualified in ocular surgery. Reply to Box 825, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

MEDICAL NEWS *in Brief*

(Continued from page 578)

NEW ORAL LONG-ACTING GANGLION-BLOCKING AGENT FOR HYPERTENSION

The substance "189c56" is chemically related to pentacynium methysulfate. When given by intravenous or subcutaneous injection, the new drug had half the effect on blood pressure of pentacynium methylsulfate. Locket (*Brit. M. J.*, 2: 74, 1958) reports 11 "long-term" cases but states that he has used the drug on many more patients over a period of more than a year. His conclusions are that this drug is invariably effective when given by mouth, that its effect is predictable and that the duration of action is much longer than with any other drug. It had much less effect on the intestinal motility and none on bladder function, and the effect on blood pressure with the patient supine was greater than with other commercially available oral ganglion-blocking drugs. Dosage has to be carefully adjusted by gradually increasing it until satisfactory control has been achieved.

—

FETISHISM IN SURGERY

In surgery as in the whole of medicine there are certain traditional manœuvres whose usefulness no one questions because they are time-honoured. Hanlon of St. Louis draws attention to some of these rituals. For example, when diffuse surface bleeding occurs, surgeons are still heard to call for "a nice hot pack" as a mechanism for local hæmostasis. If they stopped to think, they would realize that this was a throwback to the days when it was considered essential that anything touching exposed tissue should be at body temperature. For arresting bleeding, cold packs would be much more effective.

Again, says Hanlon, the use of silk instead of catgut in some surgical situations dates back to the days when catgut was made only in large sizes and was bacteriologically unsafe. Silk is no longer a fetish to ward off the evils of heavy-handed operating. — *Surg. Gynec. & Obst.*, 106: 613, 1958.

REVIEW OF FRENCH MEDICAL PUBLICATIONS

Through the courtesy of the French Embassy in Canada, a copy of a new publication entitled "The Quarterly Review of French Medical Publications" has been received. This review in the English language is prepared by Dr. Guy Godlewski of Paris and contains an abstract of the most significant French papers appearing in the previous quarter.

The first number contains references to work on steroid treatment of acute rheumatism by Mozziconacci in which he stresses the need for adequate dosage, and prophylaxis of acute rheumatism by a combination of sulfonamides and penicillin by the same author. Crime of Paris has a paper on a new antispasmodic, Lispamol, a phenothiazine derivative valuable in spastic colitis and renal colic. Levrat and Romier have treated 73 cases of infective cholelithiasis by antibiotics with good results, and Bolgert and Levy assess the results of treatment of syphilis with a combination of mercury and penicillin.

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MEDICAL NEWS *in brief*
(Continued from page 45)

Jacquelin *et al.* draw attention to development of asthma as an allergic reaction to penicillin. Kunlin and Bitry-Boely of Paris analyze 66 cases of obstruction of the bifurcation of the aorta (Leriche's syndrome), while Lapras on the basis of observations on 24 cases of frostbite recommends once more sympathetic block with procaine as the best treatment of the lesion. DeSeze discusses acroparæsthesia, and in another paper presents a complete study of 100 cases of sciatica with paralysis. Lamache notes the substantial gains from cortisone therapy in alcoholic cirrhosis of the liver and Deschamps describes an investigation of a new tranquillizer (7044 RP, or Nozinan). This drug seems most indicated in all forms of melancholia. Kupfernik considers that anorexia is the only indication for ACTH or cortisone in psychiatry.

SUICIDE AND THE LAW

In England and Wales, India and some states of the U.S.A. suicide or attempted suicide is regarded as a criminal offence. A report which has recently been issued by a joint committee of the British Medical Association and the Magistrates' Association (obtainable from the Secretary of the B.M.A.) advocates that the law in England and Wales be amended to provide that suicide and consequently attempted suicide shall no longer be a criminal offence. This recommendation excludes cases of suicide pact and incitement to suicide. It is to be hoped that the British parliament may be induced to take note of this recommendation and remove from the statute book a law which can have neither public nor medical justification, and is indeed a part of the old-fashioned apparatus for punishing the mentally afflicted. —*Brit. M. J.*, 1: 1233, 1958.

GASTROENTEROLOGICAL CONVENTION

The 23rd Annual Convention of the American College of Gastroenterology will be held at the Jung Hotel in New Orleans, La., October 20-22, 1958. In addition to the many individual papers to be presented, there will be panel discussions on gastric carcinoma, steroids in gastroenterology, and functional disturbances of the gastro-intestinal tract. There will again be scientific as well as commercial exhibits and the sessions will be open to all physicians without charge.

On October 23-25, immediately following the convention, Dr. Owen H. Wangensteen of Minneapolis, Minn., and Dr. I. Snapper of Brooklyn, N.Y., will again be the moderators of the Annual Course in Postgraduate Gastroenterology. The sessions will be held at the Jung Hotel and in the Auditorium of the Louisiana State University School of Medicine. Attendance at the course will be limited to those who have registered in advance.

As a part of this year's sessions, a one-day regional meeting will be held at the University Hospital in Mexico City on October 27, and members of the College from that city will present papers.

Copies of the program and further information concerning the Postgraduate Course and Mexico Regional Meeting may be obtained by writing to: American College of Gastroenterology, 33 West 60th St., New York 23, N.Y.

HUMAN FERTILITY

The fifth annual meeting of the Canadian Society for the Study of Fertility will take place in London, Ontario, on October 31 and November 1, 1958. Distinguished guest speakers have been invited and the topics listed range from psychiatry to radiology, including hæmatology and endocrinology. General practitioners and specialists alike are welcome. Enquiries should be directed to Dr. Jean F. Campbell, Secretary-Treasurer, 238 Queen's Avenue, London, Ontario, Canada.

POSTGRADUATE COURSES

The American College of Physicians is sponsoring the following postgraduate courses for late 1958 and early 1959: "The Physiological Basis of Internal Medicine", Duke University Medical Center, Durham, N.C., October 13 - 17; "Selected Subjects in Internal Medicine", Mayo Clinic, Rochester, Minn., November 3-7; "Gastroenterology", University of Michigan Medical School, Ann Arbor, Mich., November 10-14; "Congenital Heart Disease", Johns Hopkins University School of Medicine, Baltimore, Md., November 17-22; "Internal Medicine, with Emphasis on Therapeutics", University of Illinois College of Medicine, Chicago, Ill., January 12-16; "Current Research in Endocrinology", National Institutes of Health, Bethesda, Md., February 2-4; "Recent Advances in Cardiovascular Diseases", Mount Sinai Hospital, New York, N.Y., February 9-13; "Recent Advances in Internal Medicine", Pennsylvania Hospital, Philadelphia, Pa., February 23-27.

Further information may be obtained from E. R. Loveland, Executive Secretary, The American College of Physicians, 4200 Pine Street, Philadelphia 4, Pa.

SEMINAR IN BLOOD BANKING AND IMMUNOHAEMATOLOGY

A two-day seminar in blood banking and immunohæmatology will be held at the Royal Victoria Hospital, Montreal, Que., on October 16 and 17. The seminar is being conducted by the Ortho Research Foundation and is designed to demonstrate the newest techniques and to discuss recent advances. The program will be the same on both days. There is no registration fee.

Medical personnel who are interested in attending are asked to communicate with the Post-Graduate Board, Royal Victoria Hospital, Montreal, as soon as possible, indicating their choice of date.

AMERICAN PUBLIC HEALTH ASSOCIATION

The American Public Health Association is holding its 86th annual meeting in St. Louis, October 27 to 31. Some topics of

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MEDICAL NEWS *in brief*

(Continued from page 47)

current interest to be discussed will be atmospheric pollution in the United States; the epidemiology of events associated with ionizing radiation and its genetic and other effects; epidemiological approaches to the study of pregnancy wastage; problems in testing genetic hypotheses in human disease; detection of lung cancer by survey methods; chronic illness as a public health problem; experiences in new prepayment programs, including nursing home care, insurance against drug cost, and prepaid psychiatric services; financing of medical care for the aged, suicide as a public health problem, and sex education.

COURSES IN COMMUNICABLE DISEASE CONTROL

The Communicable Disease Center of the U.S. Public Health Service has a great number of courses in communicable disease control and related subjects scheduled to take place at the C.D.C. headquarters in Atlanta, Georgia, between September 1958 and June 1959. Detailed information may be obtained by addressing the Chief, Communicable Disease Center, U.S. Public Health Service, 50 Seventh Street, N.E., Atlanta 23, Georgia.

BRITISH ASSOCIATION OF PLASTIC SURGEONS

The British Association of Plastic Surgeons is holding an International Congress in London from July 11-17, 1959, under the Presidency of Mr. Rainsford Mowlem. The Secretary and Treasurer is Mr. David Matthews, and the address of his Secretariat to which enquiries should be addressed is: Organising Secretary, International Congress on Plastic Surgery, c/o Institute of Child Health, Hospital for Sick Children, Great Ormond Street, London, W.C.1, England.

STUDIES OF THE PARENTERAL AND TOPICAL EFFECTS OF ANTIHISTAMINES ON GASTRIC SECRETIONS

These studies were originally designed by Ragins *et al.* (*Gastroenterology*, 35: 1, 1958) to test the possibility that gastric secretion may be mediated by other substances in combination with histamine. In the course of these investigations (which involved serotonin) it was found that Neo-Antergan (pyrilamine maleate) blocked gastric secretion which usually follows stimulation of the antrum. Dogs prepared with Heidenhain pouches and with antral pouches stimulated by introduction into the antrum of a 3% suspension of desiccated liver in water reacted with an output of 15-20 mEq./l. of HCl in ½ hour. A single dose of Neo-Antergan (4 mg./kg. body weight) suppressed this response for about 1½ hours. Similar suppression was obtained with Phenergan (promethazine). Histamine-induced gastric secretion was not inhibited by intravenous Neo-Antergan or Phenergan. There was also no inhibition of the cephalic (vagal) phase of gastric secretion induced by insulin hypoglycæmia when the anti-

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throughout Canada
more than 7100 diabetics
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MEDICAL NEWS *in brief*

(Continued from page 48)

histamines were administered intravenously. On the other hand, irrigation of the pouches with a solution containing 6 mg. of Phenergan per ml. of isotonic saline suppressed free acid production after stimulation with histamine or 3% liver suspension for some three hours, and after insulin induced hypoglycæmia for about 1½ hours. Each time the volume of gastric juice was also reduced by 25-75% and the juice had an extremely high mucus content. Biopsies of gastric mucosa taken before and after topical administration of antihistamines showed that they produced local injury and the authors conclude that cell damage accounts for the reduced secretion.

—

WHO EXPERT COMMITTEE ON POLIOMYELITIS

The second report* of the WHO Expert Committee on Poliomyelitis reviews the poliomyelitis situation in 1954-57 and notes a change of pattern in the incidence of the disease. Whilst several countries which had previously suffered little from the disease reported an increased number of cases, others reported a notable reduction, attributed in most, but not in all, to mass immunization with Salk vaccine or with other vaccines of the inactivated type. Evidence is accumulating that the use of such vaccines has had a considerable effect in reducing the incidence of paralysis. However, in the U.S.A. and South Africa it was noted that vaccination did not apparently shorten the course of an epidemic, and studies have revealed that it neither prevented infection nor interfered with the dissemination of the virus.

The report also deals with the preparation and testing of vaccines, design of vaccination programs, immunity surveys, the WHO poliomyelitis program, live virus vaccines and the problems raised by enteric viruses.

The importance of filtration in ensuring a safe vaccine product is emphasized, and evidence based on experiments by the United States Technical Committee clearly

*Second Report World Health Organization: Technical Report Series, 1958, No. 145; 83 pages. Price 60 cents.

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Ferric Pyrophosphate (Soluble)	250 mg.
Iron (as Ferric Pyrophosphate)	30 mg.
Sorbitol	3.5 Gm.

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shows that more consistent results are obtained with filtration through Seitz filters than through fritted glass filters. It is pointed out, however, that repeated filtrations resulted in considerable loss of immunogenic potency. Some producers have therefore adopted other procedures to ensure consistent safety and potency, such as double inactivation with additional chemical or physical agents without filtration. The report stresses the desirability of using for vaccine production strains of low virulence provided these are of high immunogenic potency.

Antigenicity tests on the monkey have not been found to be entirely satisfactory, and further studies of other tests are recommended, including those using guinea-pigs and chicks, together with comparative studies on children lacking antibodies to all three types of poliovirus.

The Committee emphasized the importance in any vaccination program of giving relative priority to selected groups. These will generally, but not always, be the age groups showing the highest incidence. Guidance is given on other aspects of immunization programs.

The report reviews the results of immunity surveys. These are recognized as useful or even essential under certain circumstances, but generally are regarded as a poor substitute for proper reporting of paralytic cases. It was recommended that the WHO Poliomyelitis Program based on the designation of WHO Regional Laboratories should be extended to bring national laboratories into co-operation, the Regional Laboratories maintaining their functions as reference laboratories.

An important recommendation made is that live attenuated virus vaccines should be subjected to more extensive and carefully designed field trials. Great hopes were expressed regarding the potential value of such vaccines. The Committee also considered for the first time the problems raised by the numerous recently discovered enteric viruses, some of which are common causes of aseptic meningitis indistinguishable from non-paralytic poliomyelitis. It was recommended, therefore, that in poliomyelitis reporting, paralytic cases should be reported separately and that the term aseptic meningitis should be used in place of the term non-paralytic poliomyelitis.

A considerable amount of detailed information on laboratory techniques is given in the five annexes which complete this report.

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CONTROL OF GASTRIC AND PANCREATIC SECRETION BY INHIBITION OF CARBONIC ANHYDRASE

Experiments have demonstrated the presence of carbonic anhydrase in the gastric and pancreatic mucosa, and evidence has accumulated regarding the ability of carbonic anhydrase inhibitors to reduce gastric and pancreatic secretion. According to Janowitz (*Lancet*, 1: 1353, 1958), future refinement of the cholinergic-blocking antisecretory drugs is not likely to produce an ideal agent which will suppress secretion without significant side effects. On the other hand an agent which in-

(Continued on page 54)

stop "morning sickness" the night before with timed-release Bendectin 2 tabs. h.s.

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1. Nulsen, R. O.: Ohio State M. J. 53:665, 1957. 2. Personal communications, 1956-57.

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hibits carbonic anhydrase will suppress both gastric and pancreatic secretion without the side effects produced by the traditional antisecretory drugs. The author's own studies were carried out on healthy volunteers, on patients with peptic ulcers of the stomach, duodenum and jejunum (gastric secretion) and on four patients with chronic pancreatitis as well as 14 without disease of the pancreas (pancreatic secretion). In both studies the results indicate that carbonic anhydrase is intimately involved in the mechanism of secretion of hydrochloric acid (stomach) and bicarbonate (pancreas). Administration of large doses of acetazolamide by intravenous infusion was well tolerated and resulted in profound inhibition up to complete suppression of the secretion of hydrochloric acid. Similar doses were required to produce a profound inhibition of the flow of pancreatic juice and of bicarbonate output. Although safe this method is too cumbersome for general use, and oral administration of acetazolamide has proved ineffective. Further search for a more potent carbonic anhydrase inhibitor or some other agent capable of inhibiting the intracellular processes of digestive secretion is envisaged by the author.

—

BILATERAL ADRENALECTOMY IN CHRONIC SCHIZOPHRENIA

Apter of Chicago (*Am. J. Psychiat.*, 115: 55, 1958) describes a six-year follow-up of four schizophrenic patients in a state hospital who had been subjected to bilateral adrenalectomy. The original hypothesis was that adrenocortical activity might be significant as a causative factor in some cases of schizophrenia, but the follow-up did not support the hypothesis. Bilateral adrenalectomy did not appear to influence significantly the clinical course of chronic schizophrenia.

—

PROGRAMS ON ALCOHOLISM

A useful listing of programs on alcoholism research, treatment and rehabilitation in the United States and Canada has recently been published by the licensed beverage industries of the U.S.A. This is the fifth in a series published annually by the organization and contains a separate section on Canada. It lists the provincial programs in action, their activities, budgets and types of treatment facilities operated, caseloads of patients, research projects initiated during the past year and other useful information. The booklet is available from Licensed Beverage Industries, Inc., 155 East 44th Street, New York 17, N.Y., U.S.A.

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MORE AND MORE BIOPSIES

Greater and greater ingenuity is being shown in devising methods for snipping out small portions of the human body. Two recent papers describe methods for obtaining a tongue biopsy and a

digital biopsy respectively. Taft and his colleagues from Melbourne, Australia (*Lancet*, 2: 69, 1958), have devised a rigid suction-tube for tongue biopsy with an operating head. They have carried out 50 successful biopsies on 40 people whose tongues either appeared normal or showed atrophy or inflammation, without major discomfort to the patient either at operation or later. There was good correlation between the appearance of atrophy of the tongue and the biopsy findings, and the authors think that their studies may throw further light on degenerative processes in various diseases, especially as regards cellular changes. Serial biopsies on a single patient might also produce valuable evidence of the efficacy of therapy.

Phillips and Burch of Tulane University School of Medicine, New Orleans (*Am. J. M. Sc.*, 235: 668, 1958), employ a sharp skin punch to cut specimens from the finger as an adjunct in the study of the peripheral circulation. They have used this method without difficulty in over 150 patients and praise its advantages, since vascular manifestations with generalized disease appear to occur early in the fingers, while the digital biopsy can also be used to study the digital glomus bodies as well as the recently described chromaffin cells in human skin.

SUCCESSFUL TREATMENT OF ACUTE DISSEMINATED PULMONARY HISTOPLASMOSIS

While exploring a cave, a white male aged 32 years was exposed to bat manure, from which *Histoplasma capsulatum* was later isolated. Pulmonary symptoms were noted three weeks after exposure; they increased gradually in severity, and were not affected by any antibiotic therapy.

The symptoms attained their maximum severity about the time when a histoplasmin skin test became positive. The titre of complement fixation of antibodies for *Histoplasma capsulatum* in the serum was 1:128. Pulmonary rales, dyspnœa and cyanosis were severe and were not greatly alleviated by an oxygen tent.

The authors, Tegeris and Smith (*Ann. Int. Med.*, 48: 1414, 1958), felt strongly that death was imminent from mechanical obstruction of the alveoli in consequence of an allergic reaction produced by the fungi. They therefore decided to treat the patient with cortisone. The fungicidal drug beta-di-ethyl-aminoethyl-fencholate (MRD-112) was administered to prevent the dissemination of fungi. Improvement was dramatic. Cyanosis and dyspnœa disappeared in 24 hours. The patient was removed from the oxygen tent in three days. The lungs became progressively clearer and were normal roentgenographically in six months.

FATAL FUNGUS INFECTION IN SARCOIDOSIS

Reports of fatal fungal infections are appearing in the literature more frequently. This is attributed to an increase in the incidence and virulence of fungus infections in

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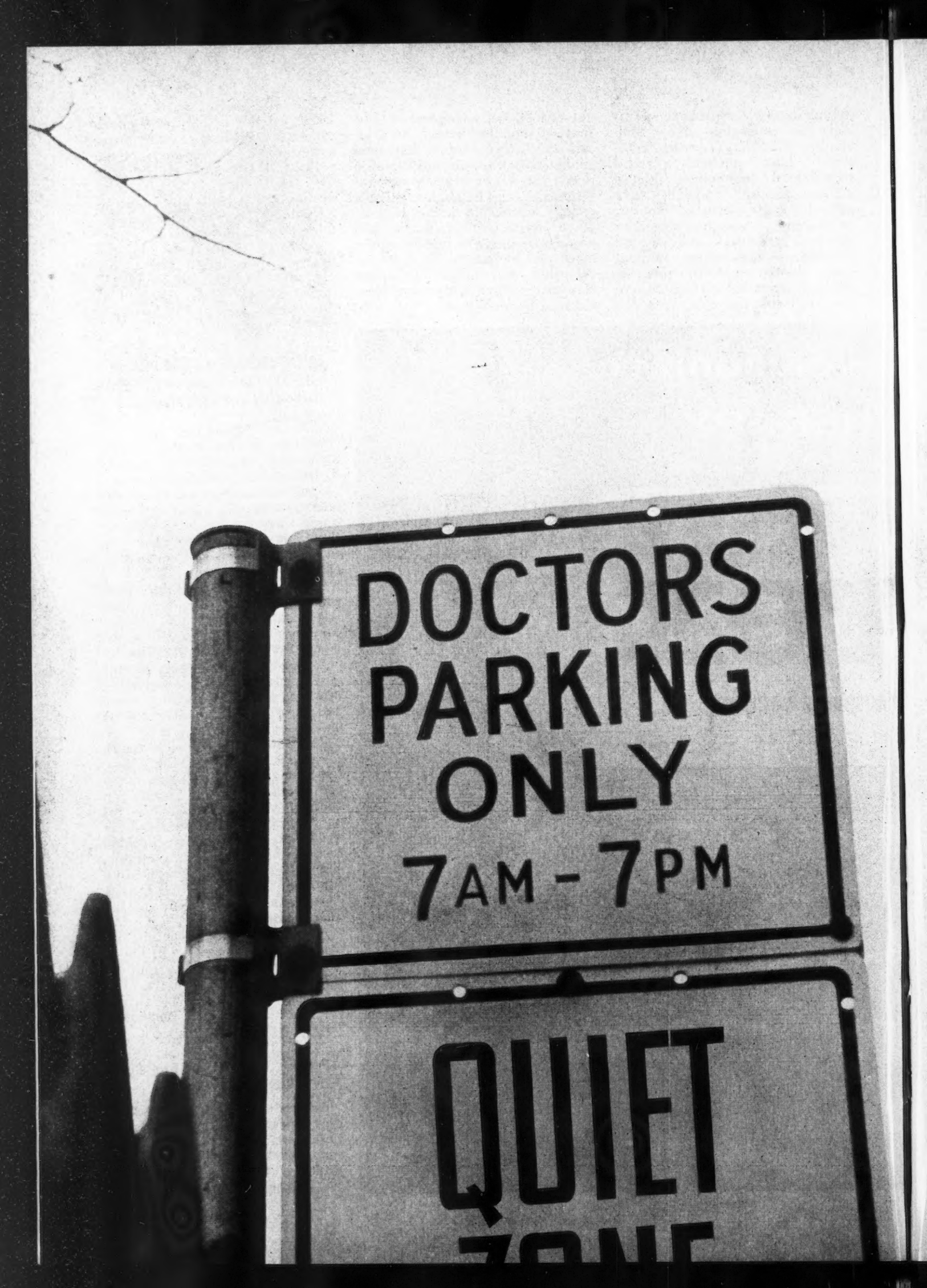
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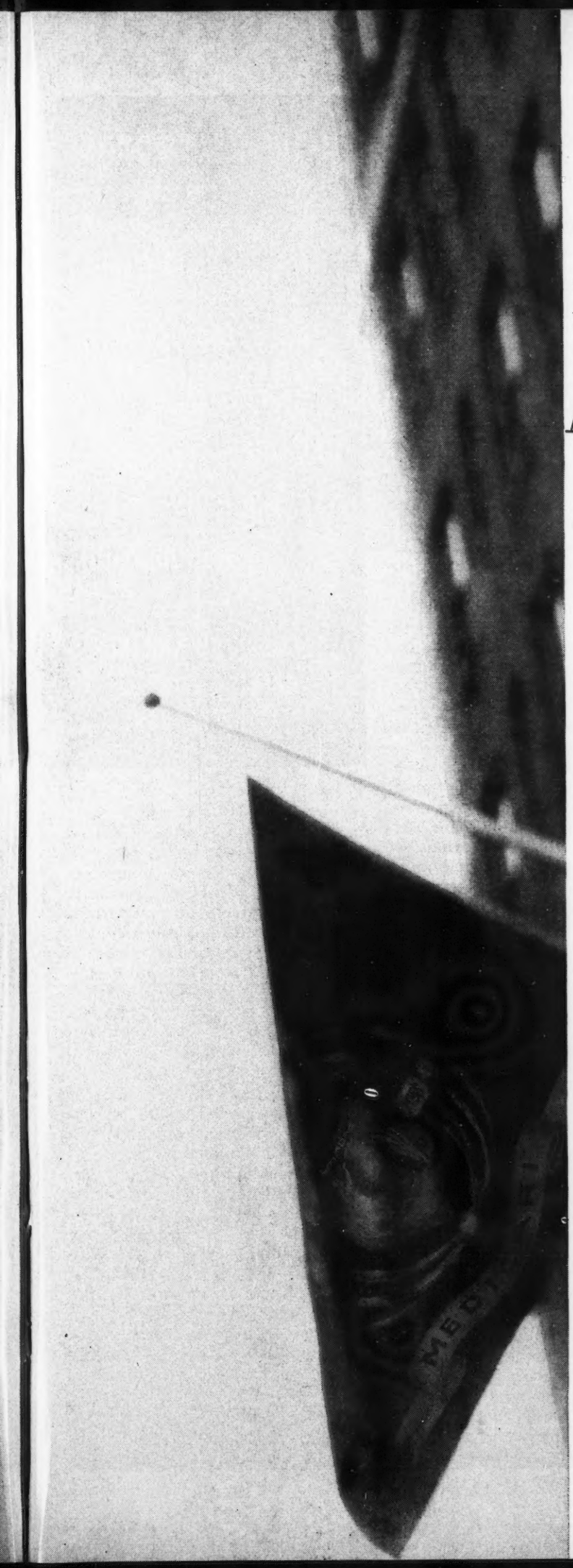

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consequence of the suppression of bacteria by antibiotics, and alterations in the reaction of infecting organisms under the influence of hormonal therapy (ACTH and cortisone). It is attributable, in part as well to improvements in the diagnosis of fungus infections, provided by modern methods of cultural and animal inoculation and new histopathologic techniques. Disseminated fungal infection has even been reported as a complication of illnesses such as aplastic anæmia, lymphoma, leukæmia, diabetes, tuberculosis and cancer.

Steinberg (*Ann. Int. Med.*, 48: 1359, 1958) reports two cases of severe pulmonary insufficiency caused by sarcoidosis with temporary amelioration of their dyspnœa after treatment with antibiotic and cortisone. In one, cerebral abscesses and meningitis caused by *Nocardia asteroides* developed. The second had repeated spontaneous pneumothoraces, which resulted from the rupture of emphysematous bullæ and were associated with the development of a broncho-cutaneous fistula and fever. Even though *Monilia albicans* was found on sputum culture, it was considered to be a contaminant. At necropsy—in addition to extensive sarcoidosis of the lung and lymph nodes—multiple lung abscesses were found, with myriads of fungi and cocci in their walls. Colonies of fungi were also found in the lumen of the broncho-cutaneous fistula.

—

SURGICAL THERAPY FOR CHRONIC NONSPECIFIC PNEUMONITIS

In 1948, the term "non-specific chronic pneumonitis" was introduced by Kershner and Adams to describe a definite pulmonary entity. From the clinical point of view, the lesion in question causes a febrile illness with insidious onset, chronic course, productive cough, pleuritic pain, and in certain cases hæmoptysis. One lobe only is usually involved and exhibits intralobular and interalveolar fibrosis, thickening of alveolar walls, lymphoid and plasma cell hyperplasia, redundancy of the bronchial mucosa, chronic atelectasis, and hæmorrhagic purulent alveolar exudate. Excision of the affected area usually results in a marked degree of improvement.

MacQuigg has advanced the theory that the disease commences as a chronic localized bronchitis, and that bronchiolar metaplasia and fibrosis subsequently develop. He considers that such cases, if untreated, will develop into typical bronchiectasis, but that antibiotics are able to arrest this progression. It is not possible to prove this theory experimentally, but clinical observations support to a certain degree MacQuigg's recommendation that resection should be considered as the treatment of choice for non-specific pneumonitis.

Denton (*Ann. Int. Med.*, 48: 1289, 1958) describes six cases in patients between 40 and 60 years of age, who had a long history of chronic pulmonary infection, with effective but partial alleviation during antibiotic therapy. Radiographs of the chest were positive in all cases for pulmonary infiltrations, shadows varying in intensity from faint to dense. Physical examination was generally less rewarding, except that most of these patients were chronically ill.

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Bronchoscopy usually revealed changes consistent with chronic bronchitis. Bronchograms were interpreted as normal, except that minimal grades of bronchiectasis were noted in two of the patients. At operation, it was found that the affected area was heavy, fibrotic and airless. Lobectomy was carried out in five cases, segmentectomy in one. The postoperative course was without complications in all these cases, and all the patients returned to a gainful occupation.

TRIAMCINOLONE IN TREATMENT OF RHEUMATOID ARTHRITIS

Hartung reports (*J. A. M. A.*, 167: 973, 1958) the treatment with a new corticosteroid of 67 patients with rheumatoid arthritis. All without exception showed unwanted side effects but most of these were minor in nature. Triamcinolone has four advantages over prednisone and the other older corticosteroids: (1) it does not produce œdema; (2) gastric irritation and peptic ulceration are less frequent; (3) psychic disturbance is minimal; and (4) there is no effect on the arterial blood presure. The author believes that this drug is the safest effective corticosteroid to date.

RESEARCH AWARDS FROM THE HEART FOUNDATIONS OF CANADA

The Heart Foundations of Canada give notice of the following types of research award: research fellowships ($3000-$6000); research associateships ($6000-$9000); and senior research associateships ($9000-$15,000).

The Heart Foundations of Canada offer support of research projects preferably of an experimental nature. This support may be either on an annual renewal basis or for a longer term as warranted. The grants are made to individual investigators and in limited numbers to groups of investigators or units working in cardiovascular research.

Application forms and regulations may be obtained from the local Provincial Heart Foundation or from the National Heart Foundation of Canada, 501 Yonge Street, Toronto 5, Ontario.

INTERNATIONAL CONGRESS ON SCHOOL AND UNIVERSITY HEALTH

The French Association of School and University Health Services is organizing the Third International Congress of School and University Health, to be held in Paris, France, on July 6, 7 and 8, 1959. The first day will be devoted to a discussion of infectious disease in a school environment; the second day to the interplay of the school environment and health; and the third day to epilepsy in the school environment. The congress will probably take place in the UNESCO building and all papers will be translated into French and English. Further information from the Secretariat, Congrès d'hygiène scolaire et universitaire, 13 rue du Four, Paris 6e, France.